

identified as AA027096 (zk04d03.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 469541 3'), AA027135 (zk04d03.r1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 469541 5'), AA166312 (ms42g11.r1 Life Tech mouse embryo 135dpc 10666014 Mus musculus cDNA clone 614276 5' similar to TRE238793 E238793 DUALIN), AA535890 (nf94a03.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA clone IMAGE:927532), H14467 (yl25g07.r1 Homo sapiens cDNA clone 159324 5' similar to contains HGR repetitive element), T21281 (Human gene signature HUMGS02637), T61016 (Total DNA sequence from cosmid clones LP(2)127 and LP(2)128), U47621 (Human nucleolar autoantigen No55 mRNA, complete cds), W51808 (zc48g04.r1 Soares senescent fibroblasts NbHSF Homo sapiens cDNA clone 325590 5' similar to PIR:S20742 S20742 synaptonemal complex protein Sc65 - rat; contains Alu repetitive element; mRNA sequence), and X97607 (G.gallus mRNA for cartilage associated protein). The predicted amino acid sequence disclosed herein for bd306\_7 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted bd306\_7 protein demonstrated at least some similarity to sequences identified as R95913 (Neural thread protein [Homo sapiens]), U47621 (nucleolar autoantigen No55 [Homo sapiens]), and X97607 (cartilage associated protein [Gallus gallus]). Two regions of bd306\_7 protein (amino acids 148-217 and 298-367 of SEQ ID NO:2) align with the same region, amino acids 145-214, of cartilage associated protein. The homology between bd306\_7 protein and nucleolar autoantigen No55 is also good, but in this case it appears that bd306\_7 amino acids 148-189 is similar to two regions of No55 (amino acids 145-186 and 296-337), and bd306\_7 amino acids 298-367 are also similar to nearly the same two regions of No55 (amino acids 145-214 and 296-365). This implies that two regions in bd306\_7 (roughly 148-189 and 298-367) are similar to each other, and one copy of this region is found in cartilage associated protein, but both are present in No55. Cartilage associated protein is reported to be localized to the extracellular matrix (J. Cell Sci 1997 110(Pt 12):1351-1359), while No55 is found in the granular component of the nucleolus (Mol Biol Cell 1996 7(7):1015-1024). Based upon sequence similarity, bd306\_7 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of bd306\_7 also indicates that it may contain an Alu repetitive element.

bd306\_7 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 52 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "fj283\_11" and Clone "fj283\_6"

Polynucleotides of the present invention have been identified as clone "fj283\_11" and clone "fj283\_6". fj283\_11 and fj283\_6 were isolated from a human adult lung carcinoma cDNA library using methods which are selective for cDNAs encoding secreted  
5 proteins (see U.S. Pat. No. 5,536,637), or were identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. fj283\_11 and fj283\_6 are full-length clones, including the entire coding sequence of a secreted protein (also referred to herein as "fj283 protein").

The nucleotide sequence of fj283\_11 as presently determined is reported in SEQ  
10 ID NO:3, and includes a poly(A) tail. The nucleotide sequence of fj283\_6 as presently determined is reported in SEQ ID NO:198, and includes a poly(A) tail. Although cDNA clones fj283\_11 and fj283\_6 have different nucleotide sequences, perhaps as a result of alternative splicing of a common primary mRNA transcript (particularly between nucleotide 402 and nucleotide 618 of SEQ ID NO:198), these clones are predicted to  
15 encode the same protein. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the fj283 protein corresponding to the foregoing nucleotide sequences is reported in SEQ ID NO:4. Amino acids 8 to 20 of SEQ ID NO:4 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 21. Due to the hydrophobic nature of the predicted  
20 leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the fj283 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone fj283\_11 should be approximately 3350 bp. The EcoRI/NotI restriction fragment  
25 obtainable from the deposit containing clone fj283\_6 should be approximately 2700 bp.

The nucleotide sequences disclosed herein for fj283\_11 and fj283\_6 were searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. fj283\_11 and/or fj283\_6 demonstrated at least some similarity with sequences identified as AA052962 (zl70c02.s1 Stratagene  
30 colon (#937204) Homo sapiens cDNA clone 509954 3' similar to gb D14531 60S RIBOSOMAL PROTEIN L9 (HUMAN)), AA080949 (zn04d12.r1 Stratagene hNT), AA160948 (zq40e12.r1 Stratagene hNT neuron (#937233) Homo sapiens cDNA clone 632206 5'), AA195089 (zr34c02.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 665282

5', mRNA sequence), AA258887 (zs32b02.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA clone IMAGE:686859 5'), H97993 (yw06e03.s1 Homo sapiens cDNA clone 251452 3'), R19768 (yg40g06.r1 Homo sapiens cDNA clone 34951 5'), U09953 (Human ribosomal protein L9 mRNA, complete cds), Z73639 (Human DNA sequence from cosmid V389H8 on chromosome X; Contains mRNA near btk gene involved in a-gamma-globulinemia, ESTs, STS), and Z73901 (Human DNA sequence from cosmid V389H8, between markers DXS366 and DXS87 on chromosome X contains pseudogene, mRNA near btk gene involved in a-gamma-globulinemia, ESTs, STS). The predicted amino acid sequence disclosed herein for the fj283 protein was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted fj283 protein demonstrated at least some similarity to sequences identified as AB011084 (KIAA0512 protein [Homo sapiens]) and U09953 (ribosomal protein L9 [Homo sapiens]). Based upon sequence similarity, fj283 proteins and each similar protein or peptide may share at least some activity. Profile hidden markov model analysis has revealed the presence of an Armadillo/beta-catenin-like domain within the predicted fj283 protein sequence. The armadillo multigene family comprises many proteins widely differing in sizes and functions which have in common a variable number of tandemly repeated arm sequences of about 42 amino acids in length. Many, but not all, armadillo-repeat-containing proteins are nuclear in localization. The predicted fj283 protein does not appear to be of the nuclear variety, but rather appears to be an extracellular protein.

#### Clone "fk317\_3"

A polynucleotide of the present invention has been identified as clone "fk317\_3". fk317\_3 was isolated from a human adult kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. fk317\_3 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "fk317\_3 protein").

The nucleotide sequence of fk317\_3 as presently determined is reported in SEQ ID NO:5, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the fk317\_3 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:6.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone fk317\_3 should be approximately 1400 bp.

The nucleotide sequence disclosed herein for fk317\_3 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
5 FASTA search protocols. fk317\_3 demonstrated at least some similarity with sequences identified as AA568588 (nm21b11.s1 NCI\_CGAP\_Co10 Homo sapiens cDNA clone IMAGE:1060797), AC002326 (Genomic sequence from Human 6, complete sequence), H48562 (yq78g07.s1 Homo sapiens cDNA clone 201948 3' similar to contains Alu repetitive element; contains MER30 repetitive element), T67164 (Human alpha-N-  
10 acetylglucosaminidase gene), and Z46941 (H.sapiens DNA for alu repeats). The predicted amino acid sequence disclosed herein for fk317\_3 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted fk317\_3 protein demonstrated at least some similarity to sequences identified as X55777 (put. ORF [Homo sapiens]). Based upon sequence similarity, fk317\_3 proteins  
15 and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the fk317\_3 protein sequence centered around amino acid 42 of SEQ ID NO:6. The nucleotide sequence of fk317\_3 indicates that it may contain an Alu repetitive element.

20 Clone "k213\_2x"

A polynucleotide of the present invention has been identified as clone "k213\_2x". Secreted cDNA clones were first isolated from a murine adult bone marrow (stromal cell line FCM-4) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or were identified as encoding a secreted  
25 or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. These murine cDNAs were then used to isolate k213\_2x, a full-length human cDNA clone, including the entire coding sequence of a secreted protein (also referred to herein as "k213\_2x protein").

The nucleotide sequence of k213\_2x as presently determined is reported in SEQ  
30 ID NO:7, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the k213\_2x protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:8. Amino acids 26 to 38 are a predicted leader/signal sequence, with the predicted mature amino



acid sequence beginning at amino acid 39. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the k213\_2x protein.

5           The EcoRI/NotI restriction fragment obtainable from the deposit containing clone k213\_2x should be approximately 1900 bp.

          The nucleotide sequence disclosed herein for k213\_2x was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. k213\_2x demonstrated at least some similarity with sequences  
10 identified as AA123852 (mp96e08.r1 Soares 2NbMT Mus musculus cDNA clone 577094 5'), AA362005 (EST71348 T-cell lymphoma Homo sapiens cDNA 5' end), AA436477 (zv08f05.s1 Soares NhHMPu S1 Homo sapiens cDNA clone 753057 3'), AA436528 (zv08f05.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 753057 5'), AA643506 (nq86f04.s1 NCI\_CGAP\_Co9 Homo sapiens cDNA clone IMAGE:1159231, mRNA  
15 sequence), F13485 (H. sapiens partial cDNA sequence; clone c-3dh08), and T19502 (Human gene signature HUMGS00560). Based upon sequence similarity, k213\_2x proteins and each similar protein or peptide may share at least some activity.

          k213\_2x protein was expressed in a COS cell expression system, and an expressed protein band of approximately 6 kDa was detected in membrane fractions using SDS  
20 polyacrylamide gel electrophoresis.

#### Clone "na316\_1"

          A polynucleotide of the present invention has been identified as clone "na316\_1". na316\_1 was isolated from a human adult brain (corpus callosum) cDNA library using  
25 methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. na316\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "na316\_1 protein").

30           The nucleotide sequence of na316\_1 as presently determined is reported in SEQ ID NO:9, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the na316\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:10. Amino

acids 30 to 42 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 43. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the na316\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone na316\_1 should be approximately 900 bp.

The nucleotide sequence disclosed herein for na316\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. No hits were found in the database. The TopPredII computer program predicts two potential transmembrane domains within the na316\_1 protein sequence, centered around amino acids 31 and 66 of SEQ ID NO:10, respectively.

#### Clone "nf93\_20"

A polynucleotide of the present invention has been identified as clone "nf93\_20". nf93\_20 was isolated from a human adult brain (substantia nigra) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nf93\_20 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nf93\_20 protein").

The nucleotide sequence of nf93\_20 as presently determined is reported in SEQ ID NO:11, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nf93\_20 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:12. Amino acids 6 to 18 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 19. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nf93\_20 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nf93\_20 should be approximately 2000 bp.

The nucleotide sequence disclosed herein for nf93\_20 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nf93\_20 demonstrated at least some similarity with sequences identified as AA063620 (ze87g07.s1 Soares fetal heart NbHH19W Homo sapiens cDNA  
5 clone 366012 3'), AA317410 (EST19337 Retina II Homo sapiens cDNA 5' end), H29417 (ym60e07.r1 Homo sapiens cDNA clone 52631 5'), and N41425 (yw93e08.r1 Homo sapiens cDNA clone 259814 5'). Based upon sequence similarity, nf93\_20 proteins and each similar protein or peptide may share at least some activity.

nf93\_20 protein was expressed in a COS cell expression system, and an expressed  
10 protein band of approximately 29 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "np164\_1"

A polynucleotide of the present invention has been identified as clone "np164\_1".  
15 np164\_1 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. np164\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred  
20 to herein as "np164\_1 protein").

The nucleotide sequence of np164\_1 as presently determined is reported in SEQ ID NO:13, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the np164\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:14. Amino  
25 acids 348 to 360 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 361. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the np164\_1 protein.

30 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone np164\_1 should be approximately 2100 bp.

The nucleotide sequence disclosed herein for np164\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and

FASTA search protocols. np164\_1 demonstrated at least some similarity with sequences identified as N63143 (yz37c12.s1 Homo sapiens cDNA clone 285238 3'), T19992 (Human gene signature HUMGS01129), Z46676 (Caenorhabditis elegans cosmid C08B11, complete sequence), and Z74910 (S.cerevisiae chromosome XV reading frame ORF YOR002w). The  
5 predicted amino acid sequence disclosed herein for np164\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted np164\_1 protein demonstrated at least some similarity to sequences identified as Z46676 (C08B11.8 [Caenorhabditis elegans]) and Z74910 (ORF YOR002w [Saccharomyces cerevisiae]). Based upon sequence similarity, np164\_1 proteins and each  
10 similar protein or peptide may share at least some activity. The TopPredII computer program predicts ten potential transmembrane domains within the np164\_1 protein sequence, centered around amino acids 4, 114, 165, 229, 293, 322, 360, 386, 436, and 465 of SEQ ID NO:14, respectively.

np164\_1 protein was expressed in a COS cell expression system, and an expressed  
15 protein band of approximately 43 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "pe204\_1"

A polynucleotide of the present invention has been identified as clone "pe204\_1".  
20 pe204\_1 was isolated from a human adult blood (chronic myelogenous leukemia K5) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pe204\_1 is a full-length clone, including the entire coding sequence of a secreted  
25 protein (also referred to herein as "pe204\_1 protein").

The nucleotide sequence of pe204\_1 as presently determined is reported in SEQ ID NO:15, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pe204\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:16. Amino  
30 acids 116 to 128 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 129. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should

the predicted leader/signal sequence not be separated from the remainder of the pe204\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pe204\_1 should be approximately 1100 bp.

5 The nucleotide sequence disclosed herein for pe204\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pe204\_1 demonstrated at least some similarity with sequences identified as AA279961 (zs92h08.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA clone 704991 3'), AA306911 (EST178043 Colon carcinoma (HCC) cell line Homo sapiens cDNA 5' end),  
10 AC002086 (Human PAC clone DJ525N14), AC002094 (Genomic sequence from Human 17, complete sequence), T97749 (ye58c04.s1 Homo sapiens cDNA clone), Z74696 (Human DNA sequence from cosmid 203C2, between markers DXS6791 and DXS8038 on chromosome X contains ESTs), Z80901 (Human DNA sequence from cosmid N119A7 on chromosome 22q12-qter), and Z82245 (Human DNA sequence \*\*\* SEQUENCING IN  
15 PROGRESS \*\*\* from clone 799F10; HTGS phase 1). The predicted amino acid sequence disclosed herein for pe204\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted pe204\_1 protein demonstrated at least some similarity to sequences identified as K02113 (Gallus gallus vitellogenin [Gallus gallus]). Based upon sequence similarity, pe204\_1 proteins and each  
20 similar protein or peptide may share at least some activity. The TopPredII computer program predicts two additional potential transmembrane domains within the pe204\_1 protein sequence, one centered around amino acid 50 and another around amino acid 90 of SEQ ID NO:16.

pe204\_1 protein was expressed in a COS cell expression system, and an expressed  
25 protein band of approximately 14 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "ya1\_1"

A polynucleotide of the present invention has been identified as clone "ya1\_1":  
30 ya1\_1 was isolated from a human adult testes cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ya1\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ya1\_1 protein").

The nucleotide sequence of ya1\_1 as presently determined is reported in SEQ ID NO:17, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ya1\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:18. Amino acids 330 to 342 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 343. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the ya1\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ya1\_1 should be approximately 1400 bp.

The nucleotide sequence disclosed herein for ya1\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ya1\_1 demonstrated at least some similarity with sequences identified as AA431507 (zw76e05.r1 Soares testis NHT Homo sapiens cDNA clone 782144 5') and F03332 (H. sapiens partial cDNA sequence; clone c-1tg07). Based upon sequence similarity, ya1\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two potential transmembrane domains within the ya1\_1 protein sequence centered around amino acid 156 and around amino acid 332 of SEQ ID NO:18, respectively. The nucleotide sequence of ya1\_1 indicates that it may contain an Alu repetitive element.

ya1\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 38 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "yb8\_1"

A polynucleotide of the present invention has been identified as clone "yb8\_1". yb8\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yb8\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yb8\_1 protein").

The nucleotide sequence of yb8\_1 as presently determined is reported in SEQ ID NO:19, and includes a poly(A) tail. What applicants presently believe to be the proper

reading frame and the predicted amino acid sequence of the yb8\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:20. Amino acids 69 to 81 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 82. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the yb8\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone yb8\_1 should be approximately 1800 bp.

The nucleotide sequence disclosed herein for yb8\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. yb8\_1 demonstrated at least some similarity with sequences identified as AA418057 (zv97a06.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 767698 5' similar to TR:G1143719 G1143719 RS-REX-B), L10334 (Homo sapiens neuroendocrine-specific protein B (NSP) mRNA, complete cds), U17603 (Rattus norvegicus rS-Rex-s mRNA, complete cds), and W19986 (zb38e09.r1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 305896 5', mRNA sequence). The predicted amino acid sequence disclosed herein for yb8\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted yb8\_1 protein demonstrated at least some similarity to sequences identified as L10334 (neuroendocrine-specific proteins B and C [Homo sapiens]) and U17603 (rS-Rex-s [Rattus norvegicus]). Based upon sequence similarity, yb8\_1 proteins and each similar protein or peptide may share at least some activity. The predicted yb8\_1 protein shows significant (60% identity) amino acid similarity to the neuro-endocrine specific protein (NSP) family of proteins. Roebroek *et al.* (1993, *J. Biol Chem.* 268: 13439, which is incorporated by reference herein) report observing three transcripts from this gene family: NSP-A (3.4 kb), -B (2.3 kb), and -C (1.8 kb); they encode proteins of 776, 356, and 208 amino acids, respectively. Roebroek *et al.* also observe that these three transcripts are identical at the 3' end and only differ over a short portion near their 5' ends, and are thus possible splice variants. NSP-A and NSP-C were found in neural and endocrine tissues while NSP-B was found only in a lung carcinoma cell line (Roebrek *et al.* state that NSP-B is "aberrant" suggesting that it might be an artifact). The C-terminal portions of the protein sequences from all three transcripts are identical. The predicted yb8\_1 protein shows

strong amino acid similarity within this region and is about as long as NSP-C. Thus the predicted yb8\_1 protein appears to be related to NSP-C. The TopPredII computer program predicts two potential transmembrane domains within the yb8\_1 protein sequence, centered around amino acids 82 and 174 of SEQ ID NO:20, respectively.

5 yb8\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 25 kDa was detected in membrane fractions and in conditioned medium using SDS polyacrylamide gel electrophoresis.

Clone "am856\_3"

10 A polynucleotide of the present invention has been identified as clone "am856\_3". am856\_3 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. am856\_3 is a full-length  
15 clone, including the entire coding sequence of a secreted protein (also referred to herein as "am856\_3 protein").

The nucleotide sequence of am856\_3 as presently determined is reported in SEQ ID NO:21, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the am856\_3 protein  
20 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:22. Amino acids 23 to 35 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 36. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the am856\_3  
25 protein. The amino acid sequence of another protein that could be encoded by basepairs 214 to 369 of SEQ ID NO:21 is reported in SEQ ID NO:274.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone am856\_3 should be approximately 2100 bp.

The nucleotide sequence disclosed herein for am856\_3 was searched against the  
30 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. am856\_3 demonstrated at least some similarity with sequences identified as M26434 (Human hypoxanthine phosphoribosyltransferase (HPRT) gene, complete cds), N71723 (yw52b09.r1 Homo sapiens cDNA clone 255833 5' similar to



gb | M87920 | HUMALNE652 Human carcinoma cell-derived Alu RNA transcript, (rRNA);  
gb X77738\_rna1 BAND 3 ANION TRANSPORT PROTEIN), U41196 (Human (TTTC)5  
short tandem repeat polymorphism UM69, D17S1339), and X89398 (H.sapiens ung gene  
for uracil DNA-glycosylase). Based upon sequence similarity, am856\_3 proteins and each  
5 similar protein or peptide may share at least some activity. The TopPredII computer  
program predicts the amino-terminal half of the am856\_3 protein sequence to be highly  
hydrophobic. The nucleotide sequence of am856\_3 indicates that it may contain one or  
more of the following types of repetitive elements: AT-like, (TTTC)5 short tandem repeat  
polymorphism UM69.

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Clone "am996\_12"

A polynucleotide of the present invention has been identified as clone "am996\_12".  
am996\_12 was isolated from a human fetal kidney cDNA library using methods which  
are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was  
15 identified as encoding a secreted or transmembrane protein on the basis of computer  
analysis of the amino acid sequence of the encoded protein. am996\_12 is a full-length  
clone, including the entire coding sequence of a secreted protein (also referred to herein  
as "am996\_12 protein").

The nucleotide sequence of am996\_12 as presently determined is reported in SEQ  
20 ID NO:23, and includes a poly(A) tail. What applicants presently believe to be the proper  
reading frame and the predicted amino acid sequence of the am996\_12 protein  
corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:24. Amino  
acids 14 to 26 are a predicted leader/signal sequence, with the predicted mature amino  
acid sequence beginning at amino acid 27. Due to the hydrophobic nature of the  
25 predicted leader/signal sequence, it is likely to act as a transmembrane domain should  
the predicted leader/signal sequence not be separated from the remainder of the  
am996\_12 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing  
clone am996\_12 should be approximately 1000 bp.

30 The nucleotide sequence disclosed herein for am996\_12 was searched against the  
GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
FASTA search protocols. No hits were found in the database. The TopPredII computer

program predicts two potential transmembrane domains within the am996\_12 protein sequence, centered around amino acids 18 and 62 of SEQ ID NO:24, respectively.

Clone "cc69\_1"

5 A polynucleotide of the present invention has been identified as clone "cc69\_1". cc69\_1 was isolated from a human adult brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. cc69\_1 is a full-length clone,  
10 including the entire coding sequence of a secreted protein (also referred to herein as "cc69\_1 protein").

The nucleotide sequence of cc69\_1 as presently determined is reported in SEQ ID NO:25, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the cc69\_1 protein corresponding  
15 to the foregoing nucleotide sequence is reported in SEQ ID NO:26.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone cc69\_1 should be approximately 550 bp.

The nucleotide sequence disclosed herein for cc69\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
20 FASTA search protocols. cc69\_1 demonstrated at least some similarity with sequences identified as AA280712 (zs98h11.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA clone IMAGE:711717 5'), AA421250 (zu27b03.s1 Soares ovary tumor NbHOT Homo sapiens cDNA clone 739181 3'), H28886 (yp03e09.s1 Homo sapiens cDNA clone 186376 3'), and H84171 (yv87c11.r1 Homo sapiens cDNA). Based upon sequence similarity, cc69\_1  
25 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the cc69\_1 protein sequence centered around amino acid 15 of SEQ ID NO:26.

Clone "cc162\_1"

30 A polynucleotide of the present invention has been identified as clone "cc162\_1". cc162\_1 was isolated from a human adult brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer

analysis of the amino acid sequence of the encoded protein. cc162\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "cc162\_1 protein").

The nucleotide sequence of cc162\_1 as presently determined is reported in SEQ ID NO:27, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the cc162\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:28. Amino acids 2 to 14 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 15. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the cc162\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone cc162\_1 should be approximately 785 bp.

The nucleotide sequence disclosed herein for cc162\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. cc162\_1 demonstrated at least some similarity with sequences identified as AA369067 (EST80419 Placenta II Homo sapiens cDNA 5' end similar to EST containing Alu repeat), L05367 (Human oligodendrocyte myelin glycoprotein (OMG) exons), and R97898 (yq60b11.r1 Homo sapiens cDNA clone 200157 5'). Based upon sequence similarity, cc162\_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of cc162\_1 indicates that it may contain one or more of the following types of repetitive elements: ALU, L1.

#### Clone "if87\_1"

A polynucleotide of the present invention has been identified as clone "if87\_1". if87\_1 was isolated from a human adult uterus cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. if87\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "if87\_1 protein").

The nucleotide sequence of if87\_1 as presently determined is reported in SEQ ID NO:29, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the if87\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:30. Amino acids 8 to 20 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 21. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the if87\_1 protein.

10. The EcoRI/NotI restriction fragment obtainable from the deposit containing clone if87\_1 should be approximately 900 bp.

The nucleotide sequence disclosed herein for if87\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. if87\_1 demonstrated at least some similarity with sequences identified as AA172949 (ms20b07.r1 Stratagene mouse skin (#937313) *Mus musculus* cDNA clone 607477 5'), AC002310 (*Homo sapiens* Chromosome 16 BAC clone CIT987-SKA-635H12 ~complete genomic sequence, complete sequence), AC003012 (Human PAC clone DJ0169K13, complete sequence), D59442 (Human fetal brain cDNA 3'-end GEN-037G12), R72810 (yl09f12.r1 *Homo sapiens* cDNA clone 157775 5' similar to contains MSR1 repetitive element), and X74358 (*P. carnea* Pod-EPPT mRNA). The predicted amino acid sequence disclosed herein for if87\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted if87\_1 protein demonstrated at least some similarity to sequences identified as Z46970 (secreted acid phosphatase 2 (SAP2) [*Leishmania mexicana*]). Based upon sequence similarity, if87\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the if87\_1 protein sequence centered around amino acid 58 of SEQ ID NO:30. The nucleotide sequence of if87\_1 indicates that it may contain one or more of the following repetitive elements: ALU, LIMA.

30 if87\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 35 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "nn103\_4"

A polynucleotide of the present invention has been identified as clone "nn103\_4". nn103\_4 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nn103\_4 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nn103\_4 protein").

The nucleotide sequence of nn103\_4 as presently determined is reported in SEQ ID NO:31, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nn103\_4 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:32. Amino acids 19 to 31 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 32. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nn103\_4 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nn103\_4 should be approximately 3500 bp.

The nucleotide sequence disclosed herein for nn103\_4 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nn103\_4 demonstrated at least some similarity with sequences identified as AA134609 (zn90e04.r1 Stratagene lung carcinoma 937218 Homo sapiens cDNA clone 565470 5'), AA584818 (no09e05.s1 NCI\_CGAP\_Phe1 Homo sapiens cDNA clone IMAGE 1100192 similar to contains L1.t1 L1 repetitive element), AC002416 (\*\*SEQUENCING IN PROGRESS\*\* Human Chromosome X; HTGS phase 1, 3 unordered pieces), AC002456 (Human BAC clone RG013L03 from 7q21, complete sequence), D25252 (Human randomly sequenced mRNA), Q05615 (Insert from pARC 1153), U95743 (Homo sapiens chromosome 16 BAC clone CIT987-SK65D3, complete sequence), Z22970 (H.sapiens mRNA for M130 antigen cytoplasmic variant 2), Z71182 (Human DNA sequence from pac 248J6, between markers DXS366 and DXS87 on chromosome X contains STS), Z81310 (Human DNA sequence from cosmid O19A on chromosome 6 Contains HLA DNA gene and STS), Z82253 (Human DNA sequence \*\* SEQUENCING

IN PROGRESS \*\*\* from clone U151E3; HTGS phase 1), and Z92547 (Human DNA sequence from PAC 863K). The predicted amino acid sequence disclosed herein for nn103\_4 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted nn103\_4 protein demonstrated at least some similarity to sequences identified as X52235 (ORFII [Homo sapiens]). Based upon sequence similarity, nn103\_4 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the nn103\_4 protein sequence centered around amino acid 52 of SEQ ID NO:32. The nucleotide sequence of nn103\_4 indicates that it may contain one or more of the following types of repetitive elements: L1, A, MER31.

#### Clone "np206\_8"

A polynucleotide of the present invention has been identified as clone "np206\_8". np206\_8 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. np206\_8 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "np206\_8 protein").

The nucleotide sequence of np206\_8 as presently determined is reported in SEQ ID NO:33, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the np206\_8 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:34.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone np206\_8 should be approximately 1900 bp.

The nucleotide sequence disclosed herein for np206\_8 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. np206\_8 demonstrated at least some similarity with sequences identified as AA126810 (zn87a12.r1 Stratagene lung cDNA), AC000053 (\*\*\* SEQUENCING IN PROGRESS \*\*\* Human Cosmid Clone 81a12 and 70g8; HTGS phase 2), AC002094 (Genomic sequence from Human 17, complete sequence), AC002431 (Human BAC clone RG180F08 from 7q31, complete sequence), F09069 (H. sapiens partial cDNA sequence; clone c-2we10), G33587 (human STS SHGC-50493), R37071 (yf66a08.s1

Homo sapiens cDNA clone 27020 3'), U91321 (Human chromosome 16p13 BAC clone), Z68746 (Human DNA sequence from cosmid Q27, chromosome region 11p15.5), and Z92846 (Human DNA sequence from cosmid U105G4, between markers DXS366 and DXS87 on chromosome X contains ESTs). Based upon sequence similarity, np206\_8  
5 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of np206\_8 indicates that it may contain one or more of the following types of repetitive elements: Alu/SVA.

Clone "nt746\_4"

10 A polynucleotide of the present invention has been identified as clone "nt746\_4". nt746\_4 was isolated from a human adult brain (corpus callosum) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nt746\_4 is a full-  
15 length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nt746\_4 protein").

The nucleotide sequence of nt746\_4 as presently determined is reported in SEQ ID NO:35, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nt746\_4 protein  
20 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:36.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nt746\_4 should be approximately 1200 bp.

The nucleotide sequence disclosed herein for nt746\_4 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
25 FASTA search protocols. nt746\_4 demonstrated at least some similarity with sequences identified as AA489740 (aa43c06.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 8236905'), J04989 (Bovine alpha 1-3 galactosyltransferase mRNA completed cds), M60263 (Human alpha-1,3-galactosyltransferase (HGT-2) pseudogene), Q74712 (Galactosyl transferase clone), R24770 (yg42c11.r1 Homo sapiens cDNA clone 35316 5' similar to SP  
30 GATR\_BOVIN P14769 N-ACETYLLACTOSAMINIDE ALPHA-1,3-GALACTOSYL-TRANSFERASE), and S71333 (alpha 1,3 galactosyltransferase [New World monkeys, mermoset lymphoid cell line B95.8, mRNA Partial, 1131 nt]). The predicted amino acid sequence disclosed herein for nt746\_4 was searched against the GenPept and GeneSeq

amino acid sequence databases using the BLASTX search protocol. The predicted nt746\_4 protein demonstrated at least some similarity to sequences identified as M26925 (galactosyltransferase (EC 2.4.1.151) [Mus musculus]), R80016 (Marmoset alpha-1,3-galactosyltransferase), S71333 (alpha 1,3 galactosyltransferase, alpha 1,3GT [New World monkeys, marmoset lymphoid cell line B95.8, Peptide, 376 aa] [Platyrrhini]), and W13639 (Murine alpha(1,3)-galactosyltransferase). Based upon sequence similarity, nt746\_4 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the nt746\_4 protein sequence centered around amino acid 15 of SEQ ID NO:36. The nucleotide sequence of nt746\_4 indicates that it may contain an LTR repetitive element.

nt746\_4 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 100 kDa was detected in conditioned medium using SDS polyacrylamide gel electrophoresis.

#### 15      Clone "pe286\_1"

A polynucleotide of the present invention has been identified as clone "pe286\_1". pe286\_1 was isolated from a human adult blood (chronic myelogenous leukemia K5) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pe286\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pe286\_1 protein").

The nucleotide sequence of pe286\_1 as presently determined is reported in SEQ ID NO:37, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pe286\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:38.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pe286\_1 should be approximately 300 bp.

The nucleotide sequence disclosed herein for pe286\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pe286\_1 demonstrated at least some similarity with sequences identified as AA588854 (no21h03.s1 NCI\_CGAP\_Pr22 Homo sapiens cDNA clone IMAGE 1101365), L46897 (Homo sapiens (subclone 3\_d9 from P1 H13) DNA sequence), and



N48057 (yy99d09.s1 Homo sapiens cDNA clone 281681 3' similar to contains element MER4 repetitive element). Based upon sequence similarity, pe286\_1 proteins and each similar protein or peptide may share at least some activity.

5        Clone "yb7\_1"

A polynucleotide of the present invention has been identified as clone "yb7\_1". yb7\_1 was isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer  
10 analysis of the amino acid sequence of the encoded protein. yb7\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yb7\_1 protein").

The nucleotide sequence of yb7\_1 as presently determined is reported in SEQ ID NO:39, and includes a poly(A) tail. What applicants presently believe to be the proper  
15 reading frame and the predicted amino acid sequence of the yb7\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:40.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone yb7\_1 should be approximately 1150 bp.

The nucleotide sequence disclosed herein for yb7\_1 was searched against the  
20 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. yb7\_1 demonstrated at least some similarity with sequences identified as N99344 (IMAGE:20090 Homo sapiens cDNA clone 20090). Based upon sequence similarity, yb7\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane  
25 domain within the yb7\_1 protein sequence located around amino acid 52 of SEQ ID NO:40; this domain is also a potential leader/signal sequence with the mature protein beginning at or near amino acid 52 of SEQ ID NO:40.

Clone "am728\_60"

30        A polynucleotide of the present invention has been identified as clone "am728\_60". am728\_60 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis

of computer analysis of the amino acid sequence of the encoded protein. am728\_60 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "am728\_60 protein").

The nucleotide sequence of am728\_60 as presently determined is reported in SEQ ID NO:41. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the am728\_60 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:42.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone am728\_60 should be approximately 4333 bp.

10 The nucleotide sequence disclosed herein for am728\_60 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. am728\_60 demonstrated at least some similarity with sequences identified as AA446039 (zw66a08.r1 Soares testis NHT Homo sapiens cDNA clone 781142 5') and U73682 (Human meningioma-expressed antigen 11 (MEA11) mRNA, partial cds).  
15 The predicted amino acid sequence disclosed herein for am728\_60 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted am728\_60 protein demonstrated at least some similarity to sequences identified as U67884 (melanoma inhibitory activity/condrocyte-derived retinoic acid sensitive protein homolog [Rattus norvegicus]), U73682  
20 (meningioma-expressed antigen 11 [Homo sapiens]), U94780 (MEA6 [Homo sapiens]), and X84707 (melanoma growth regulatory protein [Homo sapiens]). Based upon sequence similarity, am728\_60 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts three potential transmembrane domains within the am728\_60 protein sequence, centered around amino  
25 acids 300, 370, and 670 of SEQ ID NO:42, respectively.

When expressed in COS cells, am728\_60 protein was detected in a membrane fraction from these cells as a band migrating at approximately 200 kD on a denaturing SDS polyacrylamide gel.

30 Clone "bf377\_1"

A polynucleotide of the present invention has been identified as clone "bf377\_1". bf377\_1 was isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was

identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bf377\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "bf377\_1 protein").

5 The nucleotide sequence of bf377\_1 as presently determined is reported in SEQ ID NO:43, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bf377\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:44. Amino acids 27 to 39 of SEQ ID NO:44 are a predicted leader/signal sequence, with the predicted  
10 mature amino acid sequence beginning at amino acid 40. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the bf377\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing  
15 clone bf377\_1 should be approximately 450 bp.

The nucleotide sequence disclosed herein for bf377\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bf377\_1 demonstrated at least some similarity with sequences identified as AA559859 (nl48c05.s1 NCI\_CGAP\_Pr4 Homo sapiens cDNA clone IMAGE  
20 1043912), AA657838 (nu08b11.s1 NCI\_CGAP\_Pr2 Homo sapiens cDNA clone IMAGE:1207389 similar to gb:M15990 PROTO-ONCOGENE TYROSINE-PROTEIN KINASE YES (HUMAN)), and R49353 (yg67e07.s1 Homo sapiens cDNA clone 38126 3' similar to contains MER22 repetitive element). Based upon sequence similarity, bf377\_1 proteins and each similar protein or peptide may share at least some activity.

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#### Clone "cw354\_1"

A polynucleotide of the present invention has been identified as clone "cw354\_1". cw354\_1 was isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was  
30 identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. cw354\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "cw354\_1 protein").

The nucleotide sequence of cw354\_1 as presently determined is reported in SEQ ID NO:45, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the cw354\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:46. Amino acids 28 to 40 of SEQ ID NO:46 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 41. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the cw354\_1 protein.

10 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone cw354\_1 should be approximately 1350 bp.

The nucleotide sequence disclosed herein for cw354\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. cw354\_1 demonstrated at least some similarity with sequences identified as D58859 (Human placenta cDNA 5'-end GEN-514B03), H07863 (yl86b05.s1 Homo sapiens cDNA clone 45017 3'), N32178 (yy25b09.s1 Homo sapiens cDNA clone 272249 3'), R81953 (yi98e11.r1 Homo sapiens cDNA clone 147308 5'), and W84437 (zd89d06.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 356651 3'). The predicted amino acid sequence disclosed herein for cw354\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted cw354\_1 protein demonstrated at least some similarity to sequences identified as U39726 (adenosinetriphosphatase [Mycoplasma genitalium]). Based upon sequence similarity, cw354\_1 proteins and each similar protein or peptide may share at least some activity.

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#### Clone "nm134\_4"

A polynucleotide of the present invention has been identified as clone "nm134\_4". nm134\_4 was isolated from a human adult blood (erythroleukemia TF-1) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nm134\_4 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nm134\_4 protein").

The nucleotide sequence of nm134\_4 as presently determined is reported in SEQ ID NO:47, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nm134\_4 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:48. Amino acids 136 to 148 of SEQ ID NO:48 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 149. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nm134\_4 protein.

10 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nm134\_4 should be approximately 1500 bp.

The nucleotide sequence disclosed herein for nm134\_4 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nm134\_4 demonstrated at least some similarity with sequences identified as AA205020 (zq72a12.r1 Stratagene neuroepithelium (#937231) Homo sapiens cDNA clone 647134 5'), AA205286 (zq72a12.s1 Stratagene neuroepithelium (#937231) Homo sapiens cDNA clone 647134 3'), AA261864 (zs18h05.r1 Soares NbHTGBC Homo sapiens cDNA clone 685593 5'), and H63680 (yr55d03.r1 Homo sapiens cDNA clone 209189 5'). Based upon sequence similarity, nm134\_4 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts five potential transmembrane domains within the nm134\_4 protein sequence centered around amino acids 108, 132, 170, 195, and 226 of SEQ ID NO:48, respectively.

#### Clone "yb11\_1"

25 A polynucleotide of the present invention has been identified as clone "yb11\_1". yb11\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yb11\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yb11\_1 protein").

30 The nucleotide sequence of yb11\_1 as presently determined is reported in SEQ ID NO:49, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the yb11\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:50. Amino

acids 43 to 55 of SEQ ID NO:50 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 56. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the yb11\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone yb11\_1 should be approximately 2800 bp.

The nucleotide sequence disclosed herein for yb11\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. yb11\_1 demonstrated at least some similarity with sequences identified as R55695 (yg88f12.s1 Homo sapiens cDNA clone 40397 3') and R85100 (yo43b05.s1 Homo sapiens cDNA clone 180657 3'). Based upon sequence similarity, yb11\_1 proteins and each similar protein or peptide may share at least some activity.

Clone "yc2\_1"

A polynucleotide of the present invention has been identified as clone "yc2\_1". yc2\_1 was isolated from a human fetal kidney (293 cell line) cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yc2\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yc2\_1 protein").

The nucleotide sequence of yc2\_1 as presently determined is reported in SEQ ID NO:51, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the yc2\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:52. Amino acids 15 to 27 of SEQ ID NO:52 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 28. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the yc2\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone yc2\_1 should be approximately 2900 bp.

The nucleotide sequence disclosed herein for yc2\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. yc2\_1 demonstrated at least some similarity with sequences identified as AA618531 (np38a03.s1 NCL\_CGAP\_Lu1 Homo sapiens cDNA clone  
 5 IMAGE:1118572 similar to contains Alu repetitive element) and AA626937 (af84h07.s1 Soares testis NHT Homo sapiens cDNA clone 1048765 3'). Based upon sequence similarity, yc2\_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of yc2\_1 indicates that it may contain one or more Alu repetitive elements.

10

#### Clone "ff168\_12"

A polynucleotide of the present invention has been identified as clone "ff168\_12". ff168\_12 was isolated from a human adult testes (teratocarcinoma NCCIT) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat.  
 15 No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ff168\_12 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ff168\_12 protein").

The nucleotide sequence of ff168\_12 as presently determined is reported in SEQ  
 20 ID NO:53, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ff168\_12 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:54.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ff168\_12 should be approximately 1600 bp.

25 The nucleotide sequence disclosed herein for ff168\_12 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ff168\_12 demonstrated at least some similarity with sequences identified as AA025945 (ze91e02.r1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 366362 5'), AA156237 (zl50c09.s1 Soares pregnant uterus NbHPU Homo sapiens  
 30 cDNA clone 505360 3'), AA420993 (zu08e09.s1 Soares testis NHT Homo sapiens cDNA clone 731272 3'), N78486 (yz78e03.r1 Homo sapiens cDNA clone 289180 5'), W01843 (za80a01.r1 Soares fetal lung NbHL19W Homo sapiens cDNA clone 298824 5'), and W95777 (ze07e02.r1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 358298 5').

Based upon sequence similarity, ff168\_12 proteins and each similar protein or peptide may share at least some activity.

#### Clone "ls9\_1"

5 A polynucleotide of the present invention has been identified as clone "ls9\_1". ls9\_1 was isolated from a human adult brain (substantia nigra) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ls9\_1 is a full-  
10 length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ls9\_1 protein").

The nucleotide sequence of ls9\_1 as presently determined is reported in SEQ ID NO:55, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ls9\_1 protein corresponding  
15 to the foregoing nucleotide sequence is reported in SEQ ID NO:56. Amino acids 60 to 72 of SEQ ID NO:56 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 73. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the ls9\_1  
20 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ls9\_1 should be approximately 2300 bp.

The nucleotide sequence disclosed herein for ls9\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
25 FASTA search protocols. ls9\_1 demonstrated at least some similarity with sequences identified as AA527586 (ng42d05.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA clone IMAGE:937449), AC000119 (Human BAC clone RG104I04 from 7q21-7q22, complete sequence), T18551 (Human polycystic kidney disease normal PKD1 gene), Y10196 (H.sapiens PEX gene), and Z94721 (Human DNA sequence \*\*\* SEQUENCING IN  
30 PROGRESS \*\*\* from clone 167A14; HTGS phase 1). The predicted amino acid sequence disclosed herein for ls9\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted ls9\_1 protein demonstrated at least some similarity to sequences identified as AB002375 (K1AA0377



[Homo sapiens]) and R95913 (Neural thread protein). Based upon sequence similarity, ls9\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the ls9\_1 protein sequence centered around amino acid 40 of SEQ ID NO:56. The  
5 nucleotide sequence of ls9\_1 indicates that it may contain an Alu/SVA repetitive element.

#### Clone "na1010\_1"

A polynucleotide of the present invention has been identified as clone "na1010\_1". na1010\_1 was isolated from a human adult brain cDNA library using methods which are  
10 selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. na1010\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "na1010\_1 protein").

15 The nucleotide sequence of na1010\_1 as presently determined is reported in SEQ ID NO:57, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the na1010\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:58. Amino acids 24 to 36 of SEQ ID NO:58 are a predicted leader/signal sequence, with the predicted  
20 mature amino acid sequence beginning at amino acid 37. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the na1010\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing  
25 clone na1010\_1 should be approximately 1050 bp.

The nucleotide sequence disclosed herein for na1010\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. na1010\_1 demonstrated at least some similarity with sequences identified as AC002091 (Genomic sequence from Human 17, complete sequence),  
30 AC002382 (Human BAC clone RG022J17 from 7q21, complete sequence), and M26434 (Human hypoxanthine phosphoribosyltransferase (HPRT) gene, complete cds). Based upon sequence similarity, na1010\_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of na1010\_1 indicates that it may

contain one or more of the following repetitive elements: L1/A/MIR/SVA/LTRII, Alu/SVA/A/GAA, or Alu/A/GAAAA.

Clone "nf87\_1"

5 A polynucleotide of the present invention has been identified as clone "nf87\_1". nf87\_1 was isolated from a human adult brain (substantia nigra) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nf87\_1 is a full-  
10 length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nf87\_1 protein").

The nucleotide sequence of nf87\_1 as presently determined is reported in SEQ ID NO:59, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nf87\_1 protein corresponding  
15 to the foregoing nucleotide sequence is reported in SEQ ID NO:60. Amino acids 53 to 65 of SEQ ID NO:60 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 66. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nf87\_1  
20 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nf87\_1 should be approximately 1200 bp.

The nucleotide sequence disclosed herein for nf87\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
25 FASTA search protocols. nf87\_1 demonstrated at least some similarity with sequences identified as AA358277 (EST67398 Fetal lung III Homo sapiens cDNA 5' end similar to similar to interferon-alpha-inducible gene p27), W52706 (zc55g02.r1 Soares senescent fibroblasts NbHSF Homo sapiens cDNA clone 326258 5' similar to SW INI7\_HUMAN P40305 INTERFERON-ALPHA INDUCED 11.5 KD PROTEIN), and X67325 (H.sapiens  
30 p27 mRNA). The predicted amino acid sequence disclosed herein for nf87\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted nf87\_1 protein demonstrated at least some similarity to sequences identified as X67325 (p27 gene product [Homo sapiens]). The

interferon-alpha-inducible gene is localized on human chromosome 14q32 and expresses the highly hydrophobic p27 gene product in breast carcinoma cells. Based upon sequence similarity, nf87\_1 proteins and each similar protein or peptide may share at least some activity.

5 nf87\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 16 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "nh796\_1"

10 A polynucleotide of the present invention has been identified as clone "nh796\_1". nh796\_1 was isolated from a human adult brain (thalamus) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nh796\_1 is a full-  
15 length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nh796\_1 protein").

The nucleotide sequence of nh796\_1 as presently determined is reported in SEQ ID NO:61, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nh796\_1 protein  
20 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:62. Amino acids 7 to 19 of SEQ ID NO:62 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 20. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the  
25 nh796\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nh796\_1 should be approximately 1050 bp.

The nucleotide sequence disclosed herein for nh796\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
30 FASTA search protocols. nh796\_1 demonstrated at least some similarity with sequences identified as AA315985 (EST18772 Lung Homo sapiens cDNA 5' end), N23239 (yw47b07.s1 Homo sapiens cDNA clone 255349 3'), N27741 (yw51c06.s1 Homo sapiens cDNA clone 255754 3'), U69172 (Mus musculus unknown protein mRNA, complete cds),

and Z24371 (H. sapiens (D20S195) DNA segment containing (CA) repeat; clone AFM321xc1; single read). The predicted amino acid sequence disclosed herein for nh796\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted nh796\_1 protein demonstrated at least  
5 some similarity to sequences identified as U69172 (unknown [Mus musculus]). The mouse protein of unknown function (U69172) is expressed in late palate development. Based upon sequence similarity, nh796\_1 proteins and each similar protein or peptide may share at least some activity.

nh796\_1 protein was expressed in a COS cell expression system, and an expressed  
10 protein band of approximately 25 kDa was detected in conditioned media and membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "nn229\_1"

A polynucleotide of the present invention has been identified as clone "nn229\_1".  
15 nn229\_1 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nn229\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred  
20 to herein as "nn229\_1 protein").

The nucleotide sequence of nn229\_1 as presently determined is reported in SEQ ID NO:63, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nn229\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:64. Amino  
25 acids 59 to 71 of SEQ ID NO:64 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 72. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nn229\_1 protein.

30 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nn229\_1 should be approximately 1050 bp.

The nucleotide sequence disclosed herein for nn229\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and

FASTA search protocols. nn229\_1 demonstrated at least some similarity with sequences identified as H24014 (ym49f02.s1 Homo sapiens cDNA clone 51480 3'), R08508 (ye95h01.r1 Homo sapiens cDNA clone 125521 5' similar to gb|M87910|HUMALNE34 Human carcinoma cell-derived Alu RNA transcript, (rRNA); gb J02931 TISSUE FACTOR PRECURSOR (HUMAN)), and Z96508 (H.sapiens telomeric DNA sequence, clone 22QTEL030, read 22QTELOO030.seq). Based upon sequence similarity, nn229\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the nn229\_1 protein sequence centered around amino acid 20 of SEQ ID NO:64. The nucleotide sequence of nn229\_1 indicates that it may contain a MER20 repetitive element.

#### Clone "np156\_1"

A polynucleotide of the present invention has been identified as clone "np156\_1". np156\_1 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. np156\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "np156\_1 protein").

The nucleotide sequence of np156\_1 as presently determined is reported in SEQ ID NO:65, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the np156\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:66. Amino acids 6 to 18 of SEQ ID NO:66 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 19. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the np156\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone np156\_1 should be approximately 1200 bp.

The nucleotide sequence disclosed herein for np156\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. np156\_1 demonstrated at least some similarity with sequences

identified as AA298580 (EST114211 HSC172 cells I Homo sapiens cDNA 5' end), AA447514 (zw81a05.s1 Soares testis NHT Homo sapiens cDNA clone 782576 3'), AC002309 (\*\* SEQUENCING IN PROGRESS \*\* Human Chromosome 22q11 Cosmid Clone 63e9; HTGS phase 1, 3 unordered pieces), AF007269 (Arabidopsis thaliana BAC IG002N01), and N53641 (yz04g03.r1 Homo sapiens cDNA clone 282100 5'). Based upon sequence similarity, np156\_1 proteins and each similar protein or peptide may share at least some activity.

Clone "bg570\_1"

10 A polynucleotide of the present invention has been identified as clone "bg570\_1". bg570\_1 was isolated from a human adult brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bg570\_1 is a full-length clone, 15 including the entire coding sequence of a secreted protein (also referred to herein as "bg570\_1 protein").

The nucleotide sequence of bg570\_1 as presently determined is reported in SEQ ID NO:67, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bg570\_1 protein 20 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:68. Amino acids 33 to 45 of SEQ ID NO:68 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 46. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the 25 bg570\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bg570\_1 should be approximately 900 bp.

The nucleotide sequence disclosed herein for bg570\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and 30 FASTA search protocols. bg570\_1 demonstrated at least some similarity with sequences identified as T03370 (IB1429 Infant brain, Bento Soares Homo sapiens cDNA clone IB1429 3'end). Based upon sequence similarity, bg570\_1 proteins and each similar protein or peptide may share at least some activity.

Clone "bi120\_2"

A polynucleotide of the present invention has been identified as clone "bi120\_2". bi120\_2 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was  
5 identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bi120\_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "bi120\_2 protein").

The nucleotide sequence of bi120\_2 as presently determined is reported in SEQ ID  
10 NO:69, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bi120\_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:70. Amino acids 39 to 51 of SEQ ID NO:70 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 52. Due to the hydrophobic nature  
15 of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the bi120\_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bi120\_2 should be approximately 1800 bp.

20 The nucleotide sequence disclosed herein for bi120\_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bi120\_2 demonstrated at least some similarity with sequences identified as AA232119 (zr24a12.r1 Stratagene NT2 neuronal precursor 937230 Homo sapiens cDNA clone 664318 5' similar to WP:C11H1.2 CE05261), D20759 (Human HL60  
25 3'directed MboI cDNA, HUMGS01738, clone mp1051), N28753 (yx67h11.r1 Homo sapiens cDNA clone), N28806 (yx70g12.r1 Homo sapiens cDNA clone 267142 5'), N35232 (yy21d02.s1 Homo sapiens cDNA clone 271875 3'), W73805 (zd50g02.r1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 344114 5'), Z61133 (H.sapiens CpG island DNA genomic MseI fragment, clone 45g1, forward read cpg45g1.ft1a), and Z70205  
30 (Caenorhabditis elegans cosmid C11H1, complete sequence). bi120\_2 also demonstrated at least some similarity with CpG island DNA. The predicted amino acid sequence disclosed herein for bi120\_2 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted bi120\_2 protein

demonstrated at least some similarity to sequences identified as Z70205 (C11H1.2 [Caenorhabditis elegans]). Based upon sequence similarity, bi120\_2 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts five additional potential transmembrane domains within the bi120\_2 protein sequence, centered around amino acids 20, 80, 110, 150, and 290 of SEQ ID NO:70, respectively. There may be a frameshift in the full-clone sequence (somewhere within base pairs 990-1010 of SEQ ID NO:69). This frameshift from reading frame 3 to reading frame 1 would extend the open reading frame from 309 amino acids to at least 460 amino acids and add three more potential transmembrane domains to the protein. There also appears to be another frameshift occurring around base pair 1450 of SEQ ID NO:69 which shifts the open reading frame back into frame 3, adding approximately 20 more codons to the open reading frame sequence.

#### Clone "bn594\_1"

A polynucleotide of the present invention has been identified as clone "bn594\_1". bn594\_1 was isolated from a human adult placenta cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bn594\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "bn594\_1 protein").

The nucleotide sequence of bn594\_1 as presently determined is reported in SEQ ID NO:71, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bn594\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:72.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bn594\_1 should be approximately 1400 bp.

The nucleotide sequence disclosed herein for bn594\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bn594\_1 demonstrated at least some similarity with sequences identified as J03071 (Human growth hormone (GH-1 and GH-2) and chorionic somatomammotropin (CS-1, CS-2 and CS-5) genes, complete cds). Based upon sequence similarity, bn594\_1 proteins and each similar protein or peptide may share at least some



activity. The TopPredII computer program predicts a potential transmembrane domain within the bn594\_1 protein sequence centered around amino acid 52 of SEQ ID NO:72; this region is also a potential signal sequence, with the mature protein starting at amino acid 53 of SEQ ID NO:72. The nucleotide sequence of bn594\_1 indicates that it may  
5 contain one or more of the following types of repetitive elements: ALU, GAAA.

Clone "en554\_1"

A polynucleotide of the present invention has been identified as clone "en554\_1". en554\_1 was isolated from a human fetal brain cDNA library using methods which are  
10 selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. en554\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "en554\_1 protein").

15 The nucleotide sequence of en554\_1 as presently determined is reported in SEQ ID NO:73, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the en554\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:74. Amino acids 15 to 27 of SEQ ID NO:74 are a predicted leader/signal sequence, with the predicted  
20 mature amino acid sequence beginning at amino acid 28. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the en554\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing  
25 clone en554\_1 should be approximately 1800 bp.

The nucleotide sequence disclosed herein for en554\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. en554\_1 demonstrated at least some similarity with sequences identified as AA625842 (zv87d08.s1 Soares NhHMPu S1 Homo sapiens cDNA clone  
30 766767 3') and R54550 (yg75h06.r1 Homo sapiens cDNA clone 39297 5'). Based upon sequence similarity, en554\_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of en554\_1 indicates that it may contain repetitive elements in the region between base pairs 849 and 1023 of SEQ ID NO:73.

Clone "na474\_10"

A polynucleotide of the present invention has been identified as clone "na474\_10". na474\_10 was isolated from a human adult brain (corpus callosum) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. na474\_10 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "na474\_10 protein").

The nucleotide sequence of na474\_10 as presently determined is reported in SEQ ID NO:75, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the na474\_10 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:76. Amino acids 69 to 81 of SEQ ID NO:76 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 82. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the na474\_10 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone na474\_10 should be approximately 1500 bp.

The nucleotide sequence disclosed herein for na474\_10 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. na474\_10 demonstrated at least some similarity with sequences identified as AA262604 (zs23f01.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA clone IMAGE:686041 3' similar to contains Alu repetitive element), AA450131 (zx42a02.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 789098 5'), U72661 (Human ninjurin1 mRNA, complete cds), and W38567 (zb20h04.r1 Soares fetal lung NbHL19W Homo sapiens cDNA clone 302647 5'). The predicted amino acid sequence disclosed herein for na474\_10 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted na474\_10 protein demonstrated at least some similarity to sequences identified as U72661 (ninjurin1 [Homo sapiens]). Based upon sequence similarity, na474\_10 proteins and each similar protein or peptide may share at least some activity. Ninjurin is a cell-surface protein and adhesion molecule which is induced by nerve injury and promotes axonal growth.

Ninjurin is capable of mediating homophilic adhesion and can promote neurite extension of dorsal root ganglion neurons *in vitro*. It is thought to play a role in nerve regeneration and in the formation and function of other tissues (Araki *et al.*, 1996, *Neuron* 17(2):353-361, incorporated herein by reference). na474\_10 and ninjurin appear to define a novel family of adhesion molecules.

na474\_10 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 15 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

#### 10      Clone "nn16\_10"

A polynucleotide of the present invention has been identified as clone "nn16\_10". nn16\_10 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nn16\_10 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nn16\_10 protein").

The nucleotide sequence of nn16\_10 as presently determined is reported in SEQ ID NO:77, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nn16\_10 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:78. Amino acids 14 to 26 of SEQ ID NO:78 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 27. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nn16\_10 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nn16\_10 should be approximately 1600 bp.

The nucleotide sequence disclosed herein for nn16\_10 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nn16\_10 demonstrated at least some similarity with sequences identified as R46973 (Y224 *Rattus norvegicus* cDNA clone Y224 5' end), U43404 (*Sus scrofa* ameloblastin mRNA, complete cds), W13000 (mb21d12.r1 Soares mouse

p3NMF19.5 *Mus musculus* cDNA clone 330071 5'), and W36463 (mb71c12.r1 Soares mouse p3NMF19.5 *Mus musculus* cDNA clone 334870 5'). The predicted amino acid sequence disclosed herein for nn16\_10 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted  
5 nn16\_10 protein demonstrated at least some similarity to sequences identified as U43404 (ameloblastin [*Sus scrofa*]), and to the ameloblastin proteins of rat (and other species). Ameloblastin is a unique ameloblast-specific gene product that may be important in enamel matrix formation and mineralization (Krebsbach *et al.*, 1996, *J. Biol. Chem.* 271: 4431, incorporated herein by reference). Rat ameloblastin is 442 amino acids and is a  
10 tooth-specific enamel matrix protein. Immunohistochemical data show staining of golgi and of secretory granules of the secretory ameloblast, in addition to the entire thickness of the enamel matrix. The rat ameloblastin protein is synthesized as a 55 kDa core protein which undergoes extensive post-translational modifications with O-linked oligo-  
15 *Cytochem.* 45(10):1329-1340, incorporated herein by reference). Based upon sequence similarity, nn16\_10 proteins and each similar protein or peptide may share at least some activity.

nn16\_10 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 84 kDa was detected in conditioned medium and  
20 membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "np189\_9"

A polynucleotide of the present invention has been identified as clone "np189\_9". np189\_9 was isolated from a human fetal kidney (293 cell line) cDNA library using  
25 methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. np189\_9 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "np189\_9 protein").

30 The nucleotide sequence of np189\_9 as presently determined is reported in SEQ ID NO:79, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the np189\_9 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:80. Amino

acids 41 to 53 of SEQ ID NO:80 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 54. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the np189\_9 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone np189\_9 should be approximately 2100 bp.

The nucleotide sequence disclosed herein for np189\_9 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. np189\_9 demonstrated at least some similarity with sequences identified as AA035196 (zk27f12.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 471791 3'), AA336568 (EST41447 Endometrial tumor Homo sapiens cDNA 5' end), AA420972 (zt86a11.s1 Soares testis NHT Homo sapiens cDNA clone 729212 3'), and H38460 (yp69h08.s1 Homo sapiens cDNA clone 192735 3'). Based upon sequence similarity, np189\_9 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the np189\_9 protein sequence centered around amino acid 38 of SEQ ID NO:80.

#### Clone "ny226\_1"

A polynucleotide of the present invention has been identified as clone "ny226\_1". ny226\_1 was isolated from a human adult brain (substantia nigra) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ny226\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ny226\_1 protein").

The nucleotide sequence of ny226\_1 as presently determined is reported in SEQ ID NO:81, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ny226\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:82.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ny226\_1 should be approximately 3175 bp.

The nucleotide sequence disclosed herein for ny226\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ny226\_1 demonstrated at least some similarity with sequences identified as AC002463 (Human BAC clone RG302F04 from 7q31, complete sequence),  
5 R07637 (ye98e03.s1 Homo sapiens cDNA clone 125788 3'), and Z78730 (H.sapiens flow-sorted chromosome 6 HindIII fragment, SC6pA15C3). Based upon sequence similarity, ny226\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the ny226\_1 protein sequence centered around amino acid 22 of SEQ ID NO:82;  
10 this region is also a putative signal sequence, with the mature protein starting at amino acid 23 of SEQ ID NO:82. The nucleotide sequence of ny226\_1 indicates that it may contain one or more repetitive elements, including ALU repetitive elements.

Clone "pe159\_1"

15 A polynucleotide of the present invention has been identified as clone "pe159\_1". pe159\_1 was isolated from a human adult blood (chronic myelogenous leukemia K5) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded  
20 protein. pe159\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pe159\_1 protein").

The nucleotide sequence of pe159\_1 as presently determined is reported in SEQ ID NO:83, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pe159\_1 protein  
25 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:84.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pe159\_1 should be approximately 1000 bp.

The nucleotide sequence disclosed herein for pe159\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
30 FASTA search protocols. pe159\_1 demonstrated at least some similarity with sequences identified as AA372974 (EST84925 Colon adenocarcinoma IV Homo sapiens cDNA 5' end), AC002377 (Human PAC clone Dj222H05), AC002519 (\*\* SEQUENCING IN PROGRESS \*\* Human chromosome 16p11.2 BAC clone CIT987SK-A-355G7; HTGS phase

2, 1 ordered pieces), H45355 (yn99b01.r1 Homo sapiens cDNA clone 176521 5'), W39648 (zc19c09.r1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 322768 5'), and Z84816 (Human DNA sequence from PAC 2A2 on chromosome X contains ESTs). The predicted amino acid sequence disclosed herein for pe159\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted pe159\_1 protein demonstrated at least some similarity to sequences identified as M84237 (integrin beta-1 subunit [Homo sapiens]) and R96800 (Human histiocyte-secreted factor HSF). Based upon sequence similarity, pe159\_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of pe159\_1 indicates that it may contain one or more of the following types of repetitive elements: Alu, SVA, MER3.

#### Clone "pj314\_8"

A polynucleotide of the present invention has been identified as clone "pj314\_8". pj314\_8 was isolated from a human fetal carcinoma (cell type NTD2 treated with retinoic acid for 23 days) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pj314\_8 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pj314\_8 protein").

The nucleotide sequence of pj314\_8 as presently determined is reported in SEQ ID NO:85, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pj314\_8 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:86. Amino acids 23 to 35 of SEQ ID NO:86 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 36. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the pj314\_8 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pj314\_8 should be approximately 1200 bp.

The nucleotide sequence disclosed herein for pj314\_8 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and

FASTA search protocols. pj314\_8 demonstrated at least some similarity with sequences identified as H98510 (yv90g02.r1 Homo sapiens cDNA clone), U03019 (Human melanoma growth stimulatory activity beta (MGSA beta) gene, partial cds), U25660 (Dictyostelium discoideum actin gene, partial cds), W67504 (zd40f09.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 343145 3'), Z99358 (Homo sapiens mRNA; expressed sequence tag; clone DKFZphamy1\_1a3, 5' read), and Z99359 (Homo sapiens mRNA; expressed sequence tag; clone DKFZphamy1\_1a3, 3' read). The predicted amino acid sequence disclosed herein for pj314\_8 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted pj314\_8 protein demonstrated at least some similarity to sequences identified as U16359 (nitric oxide synthase [Rattus norvegicus]). Based upon sequence similarity, pj314\_8 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of pj314\_8 indicates that it may contain one or more of the following types of repetitive elements: AC repeats, PAB repeats, CA repeats.

#### Clone "bp870\_1"

A polynucleotide of the present invention has been identified as clone "bp870\_1". bp870\_1 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bp870\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "bp870\_1 protein").

The nucleotide sequence of bp870\_1 as presently determined is reported in SEQ ID NO:87, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bp870\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:88. Amino acids 9 to 21 of SEQ ID NO:88 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 22. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the bp870\_1 protein.



The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bp870\_1 should be approximately 1000 bp.

The nucleotide sequence disclosed herein for bp870\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bp870\_1 demonstrated at least some similarity with sequences identified as AA229935 (nc51g10.r1 NCI\_CGAP\_Pr3 Homo sapiens cDNA clone IMAGE:1011714 similar to contains Alu repetitive element; contains element MER4 repetitive element), H12643 (yj13a04.r1 Homo sapiens cDNA clone 1485905'), and H12594 (yj13a04.s1 Homo sapiens cDNA clone 148590 3' similar to contains Alu repetitive element). Based upon sequence similarity, bp870\_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of bp870\_1 indicates that it may contain a simple repeat region and at least one copy of an Alu repetitive element.

bp870\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 23 kDa was detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "bx141\_2"

A polynucleotide of the present invention has been identified as clone "bx141\_2". bx141\_2 was isolated from a human adult ovary (PA-1 teratocarcinoma, pool of retinoic-acid-treated, activin-treated, and untreated tissue) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bx141\_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "bx141\_2 protein").

The nucleotide sequence of bx141\_2 as presently determined is reported in SEQ ID NO:89, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bx141\_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:90. Amino acids 30 to 42 of SEQ ID NO:90 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 43. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain

should the predicted leader/signal sequence not be separated from the remainder of the bx141\_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bx141\_2 should be approximately 1800 bp.

5       The nucleotide sequence disclosed herein for bx141\_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bx141\_2 demonstrated at least some similarity with sequences identified as AA173353 (zp32b01.r1 Stratagene neuroepithelium (#937231) Homo sapiens cDNA clone 611113 5' similar to SW:A15\_HUMAN P41732 CELL SURFACE  
10 GLYCOPROTEIN A15), AA375927 (EST88303 HSC172 cells II Homo sapiens cDNA 5' end similar to similar to cell surface glycoprotein), D10653 (Human mRNA for cell surface glycoprotein, complete cds), H64050 (yr58c07.r1 Homo sapiens cDNA clone 209484 5' similar to SP:S39262 S39262 PLATELET CELL SURFACE GLYCOPROTEIN), and R41866 (yg12f04.s1 Homo sapiens cDNA clone 31854 3'). The predicted amino acid sequence  
15 disclosed herein for bx141\_2 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted bx141\_2 protein demonstrated at least some similarity to sequences identified as D10653 (HUMA15\_1 cell surface glycoprotein [Homo sapiens]) and D29808 (HUMTALLA1\_1 TALLA-1 [Homo sapiens]). The human cell surface glycoprotein ("D10653 protein") is a protein of 244  
20 amino acids which contains four potential transmembrane domains and four possible N-linked glycosylation sites. A computer-aided comparison showed a marked similarity between D10653 protein and several other membrane proteins: CD9, CD37, CD53, TAPA-1, Sm23, CO-029, and ME491/CD63; also, D10653 protein is similar to the ME491/CD63 protein superfamily. bx141\_2 protein also shows some similarity to the  
25 human and mouse ME491 and CD63 proteins. Based upon sequence similarity, bx141\_2 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts four potential transmembrane domains within the bx141\_2 protein sequence centered around amino acids 31, 70, 104, and 222 of SEQ ID NO:90, respectively.

30       bx141\_2 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 24 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "cw272\_7"

A polynucleotide of the present invention has been identified as clone "cw272\_7". cw272\_7 was isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was  
5 identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. cw272\_7 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "cw272\_7 protein").

The nucleotide sequence of cw272\_7 as presently determined is reported in SEQ  
10 ID NO:91, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the cw272\_7 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:92. Amino acids 48 to 60 of SEQ ID NO:92 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 61. Due to the hydrophobic nature  
15 of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the cw272\_7 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone cw272\_7 should be approximately 2300 bp.

20 The nucleotide sequence disclosed herein for cw272\_7 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. While no clear hits were found in these databases, cw272\_7 protein does show some similarity to bone morphogenetic proteins and procollagens.

Clone "nh328\_5"

25 A polynucleotide of the present invention has been identified as clone "nh328\_5". nh328\_5 was isolated from a human adult brain (thalamus) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of  
30 computer analysis of the amino acid sequence of the encoded protein. nh328\_5 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nh328\_5 protein").

The nucleotide sequence of nh328\_5 as presently determined is reported in SEQ ID NO:93, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nh328\_5 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:94. Amino acids 60 to 72 of SEQ ID NO:94 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 73. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nh328\_5 protein.

10 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nh328\_5 should be approximately 2200 bp.

The nucleotide sequence disclosed herein for nh328\_5 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nh328\_5 demonstrated at least some similarity with sequences identified as AA426157 (zv83a09.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 760216 5'), D17160 (Human HepG2 3' region MboI cDNA, clone hmd2d01m3), D56329 (Human fetal brain cDNA 5'-end GEN-424F08), N62903 (yy67e09.s1 Homo sapiens cDNA clone 278632 3'), R88485 (ym94e01.r1 Homo sapiens cDNA clone 166584 5'), and T26592 (AB329E6R Homo sapiens cDNA clone LLAB329E6 5'). Based upon sequence similarity, nh328\_5 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of nh328\_5 indicates that it may contain some GAA/TIGGER repeat sequences.

nh328\_5 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 70 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "nm214\_3"

A polynucleotide of the present invention has been identified as clone "nm214\_3". nm214\_3 was isolated from a human adult blood (erythroleukemia TF-1) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nm214\_3

is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nm214\_3 protein").

The nucleotide sequence of nm214\_3 as presently determined is reported in SEQ ID NO:95, and includes a poly(A) tail. What applicants presently believe to be the proper  
5 reading frame and the predicted amino acid sequence of the nm214\_3 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:96.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nm214\_3 should be approximately 1300 bp.

The nucleotide sequence disclosed herein for nm214\_3 was searched against the  
10 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nm214\_3 demonstrated at least some similarity with sequences identified as D10083 (Human RGH1 gene), D11078 (Human RGH2 gene), R68638 (y106g11.s1 Homo sapiens cDNA clone 1385003'), U88895 (Human endogenous retrovirus H D1 leader region/integrase-derived ORF1, ORF2, and putative envelope protein  
15 mRNA, complete cds), Z95327 (Human DNA sequence \*\*\*SEQUENCING IN PROGRESS \*\*\* from clone 347M6; HTGS phase 1), and Z97183 (Human DNA sequence \*\*\*SEQUENCING IN PROGRESS \*\*\* from clone ICB2046; HTGS phase 1). The predicted amino acid sequence disclosed herein for nm214\_3 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The  
20 predicted nm214\_3 protein demonstrated at least some similarity to sequences identified as U88895 (HERV-H integrase/envelope region [Homo sapiens]). Based upon sequence similarity, nm214\_3 proteins and each similar protein or peptide may share at least some activity. The nm214\_3 protein has a putative signal sequence at amino acids 13 to 25 of SEQ ID NO:96, with the mature protein starting at amino acid 26. The TopPredII  
25 computer program predicts a potential transmembrane domain within the nm214\_3 protein sequence centered around amino acid 90 of SEQ ID NO:96.

nm214\_3 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 13 kDa was detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

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#### Clone "nn320\_2"

A polynucleotide of the present invention has been identified as clone "nn320\_2". nn320\_2 was isolated from a human fetal kidney (293 cell line) cDNA library using

methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nn320\_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nn320\_2 protein").

The nucleotide sequence of nn320\_2 as presently determined is reported in SEQ ID NO:97, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nn320\_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:98. Amino acids 4 to 16 of SEQ ID NO:98 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 17. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nn320\_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nn320\_2 should be approximately 2500 bp.

The nucleotide sequence disclosed herein for nn320\_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nn320\_2 demonstrated at least some similarity with sequences identified as AA423969 (zv79h04.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 759895 5') and AA423988 (zv79h04.s1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 759895 3'). The predicted amino acid sequence disclosed herein for nn320\_2 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted nn320\_2 protein demonstrated at least some similarity to sequences identified as M60351 (filamentous hemagglutinin [Bordetella pertussis]) and R05041 (Filamentous haemagglutinin A). The predicted nn320\_2 protein also demonstrated similarity to a variety of proteases and enzyme precursors such as trypsinogen precursor. Based upon sequence similarity, nn320\_2 proteins and each similar protein or peptide may share at least some activity.

nn320\_2 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 58 kDa was detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "pp392\_3"

A polynucleotide of the present invention has been identified as clone "pp392\_3". pp392\_3 was isolated from a human adult blood (lymphoblastic leukemia MOLT-4) cDNA library using methods which are selective for cDNAs encoding secreted proteins  
5 (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pp392\_3 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pp392\_3 protein").

The nucleotide sequence of pp392\_3 as presently determined is reported in SEQ  
10 ID NO:99, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pp392\_3 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:100.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pp392\_3 should be approximately 2100 bp.

15 The nucleotide sequence disclosed herein for pp392\_3 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pp392\_3 demonstrated at least some similarity with sequences identified as AA117686 (mo64c07.r1 Stratagene mouse heart (#937316) Mus musculus cDNA clone 558348 5') and AL008726 (Human DNA sequence \*\*\* SEQUENCING IN  
20 PROGRESS \*\*\* from clone 337O18; HTGS phase 1). Based upon sequence similarity, pp392\_3 proteins and each similar protein or peptide may share at least some activity. The pp392\_3 protein has a putative signal sequence at amino acids 196 to 208 of SEQ ID NO:100, with the mature protein starting at amino acid 209. The TopPredII computer program predicts three potential transmembrane domains within the pp392\_3 protein  
25 sequence centered around amino acids 20, 130, and 310 of SEQ ID NO:100, respectively.

The nucleotide sequence of pp392\_3 indicates that it may contain a CA repetitive element.

pp392\_3 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 56 kDa was detected in membrane fractions using SDS  
30 polyacrylamide gel electrophoresis.

Clone "ya13\_1"

A polynucleotide of the present invention has been identified as clone "ya13\_1". ya13\_1 was isolated from a human adult testes cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ya13\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ya13\_1 protein").

The nucleotide sequence of ya13\_1 as presently determined is reported in SEQ ID NO:101, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ya13\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:102. Amino acids 72 to 84 of SEQ ID NO:102 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 85. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the ya13\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ya13\_1 should be approximately 750 bp.

The nucleotide sequence disclosed herein for ya13\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ya13\_1 demonstrated at least some similarity with sequences identified as AA190721 (zp88a07.r1 Stratagene HeLa cell s3 937216 Homo sapiens cDNA clone 627252 5'). Based upon sequence similarity, ya13\_1 proteins and each similar protein or peptide may share at least some activity.

Clone "yb37\_1"

A polynucleotide of the present invention has been identified as clone "yb37\_1". yb37\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yb37\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yb37\_1 protein").

The nucleotide sequence of yb37\_1 as presently determined is reported in SEQ ID NO:103, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the yb37\_1 protein



corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:104. Amino acids 28 to 40 of SEQ ID NO:104 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 41. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the yb37\_1 protein. The TopPredII computer program predicts an additional potential transmembrane domain within the yb37\_1 protein sequence centered around amino acid 144 of SEQ ID NO:104.

Another possible reading frame and predicted amino acid sequence encoded by yb37\_1 is reported in SEQ ID NO:275; amino acids 49 to 61 of SEQ ID NO:275 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 62. Due to the hydrophobic nature of this predicted leader/signal sequence, it is likely to act as a transmembrane domain should it not be separated from the remainder of the protein of SEQ ID NO:275.

The nucleotide sequence disclosed herein for yb37\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. No hits were found in the database. The nucleotide sequence of yb37\_1 indicates that it may contain one or more A/TAAA repetitive elements.

yb37\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 33 kDa was detected in conditioned medium fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "yb39\_1"

A polynucleotide of the present invention has been identified as clone "yb39\_1". yb39\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yb39\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yb39\_1 protein").

The nucleotide sequence of yb39\_1 as presently determined is reported in SEQ ID NO:105, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the yb39\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:106. Amino acids 21 to 33 of SEQ ID NO:106 are a predicted leader/signal sequence, with the

predicted mature amino acid sequence beginning at amino acid 34. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the yb39\_1 protein.

5 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone yb39\_1 should be approximately 825 bp.

The nucleotide sequence disclosed herein for yb39\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. No hits were found in the database.

10

Clone "bd577\_1"

A polynucleotide of the present invention has been identified as clone "bd577\_1". bd577\_1 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was  
15 identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bd577\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "bd577\_1 protein").

The nucleotide sequence of bd577\_1 as presently determined is reported in SEQ  
20 ID NO:107, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bd577\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:108. Amino acids 42 to 54 of SEQ ID NO:108 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 55. Due to the  
25 hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the bd577\_1 protein.

Another possible reading frame and predicted amino acid sequence encoded by base pairs 23 to 412 of bd577\_1 SEQ ID NO:107 is reported in SEQ ID NO:276; the amino  
30 acid sequence of SEQ ID NO:276 has a possible signal sequence from amino acids 57 to 69, with the predicted mature amino acid sequence beginning at amino acid 70. The open reading frames corresponding to SEQ ID NO:276 and SEQ ID NO:108 could be joined if a frameshift were introduced into the nucleotide sequence of SEQ ID NO:107.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bd577\_1 should be approximately 1800 bp.

The nucleotide sequence disclosed herein for bd577\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bd577\_1 demonstrated at least some similarity with sequences identified as AA306618 (EST177563 Jurkat T-cells VI Homo sapiens cDNA 5' end) and R20055 (yg39b06.r1 Homo sapiens cDNA clone 348055'). Based upon sequence similarity, bd577\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two potential transmembrane domains within the bd577\_1 protein sequence centered around amino acids 42 and 230 of SEQ ID NO:108.

bd577\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 56 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

#### 15      Clone "bv280\_3"

A polynucleotide of the present invention has been identified as clone "bv280\_3". bv280\_3 was isolated from a human adult brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bv280\_3 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "bv280\_3 protein").

The nucleotide sequence of bv280\_3 as presently determined is reported in SEQ ID NO:109, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bv280\_3 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:110. Amino acids 10 to 22 of SEQ ID NO:110 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 23. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the bv280\_3 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bv280\_3 should be approximately 1900 bp.

The nucleotide sequence disclosed herein for bv280\_3 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bv280\_3 demonstrated at least some similarity with sequences identified as AA095665 (l5468.seq.F Fetal heart, Lambda ZAP Express Homo sapiens cDNA 5'), AA577430 (nm96g10.s1 NCI\_CGAP\_Co9 Homo sapiens cDNA clone IMAGE:1076130 similar to TR:G945383 G945383 CARBOXYPEPTIDASE), F06654 (H. sapiens partial cDNA sequence; clone c-1ga12), F08501 (H. sapiens partial cDNA), and H10119 (ym03f03.r1 Homo sapiens cDNA clone 46734 5' similar to SP:A41612 A41612 VITELLOGENIC CARBOXYPEPTIDASE). The predicted amino acid sequence disclosed herein for bv280\_3 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted bv280\_3 protein demonstrated at least some similarity to sequences identified as L46594 (carboxypeptidase [Aedes aegypti]) and R96737 (A. niger Bo-1 carboxypeptidase Y). Based upon sequence similarity, bv280\_3 proteins and each similar protein or peptide may share at least some activity. The bv280\_3 protein also has a serine carboxypeptidase active site motif (residues 195-212). This motif is highly specific to serine carboxypeptidases and is not found in any other type of protein in the Swiss-Prot database. The bv280\_3 protein also has one copy of the crystallins beta and gamma 'Greek key' motif signature. The TopPredII computer program predicts another potential transmembrane domain within the bv280\_3 protein sequence centered around amino acid 110 of SEQ ID NO:110.

bv280\_3 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 61 kDa was detected in conditioned medium fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "co315\_3"

A polynucleotide of the present invention has been identified as clone "co315\_3". co315\_3 was isolated from a human adult brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. co315\_3 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "co315\_3 protein").

The nucleotide sequence of co315\_3 as presently determined is reported in SEQ ID NO:111, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the co315\_3 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:112.

- 5 Amino acids 51 to 63 of SEQ ID NO:112 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 64. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the co315\_3 protein.

- 10 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone co315\_3 should be approximately 710 bp.

- The nucleotide sequence disclosed herein for co315\_3 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. co315\_3 demonstrated at least some similarity with sequences
- 15 identified as AA031371 (zk15e11.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 470636 3'), AA026051 (ze86a07.s1 Soares fetal heart NbHH19W Homo sapiens), AA393961 (zt78b10.r1 Soares testis NHT Homo sapiens cDNA clone 728443 5'), AA481047 (aa29c06.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA clone IMAGE:814666 3'), H46323 (yo15c05.r1 Homo sapiens cDNA clone 177992 5'), N23329 (yx78h09.s1 Homo sapiens
- 20 cDNA clone 267905 3'), and R43942 (yg22f02.s1 Homo sapiens cDNA clone 33080 3' similar to gb:M14648 VITRONECTIN RECEPTOR ALPHA SUBUNIT PRECURSOR (HUMAN)). Based upon sequence similarity, co315\_3 proteins and each similar protein or peptide may share at least some activity.

- 25 Clone "ij226\_6"

A polynucleotide of the present invention has a nucleotide sequence as follows:

The nucleotide sequence of ij226\_6 as presently determined is reported in SEQ ID NO:113, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ij226\_6 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:114.

5 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ij226\_6 should be approximately 2300 bp.

The nucleotide sequence disclosed herein for ij226\_6 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ij226\_6 demonstrated at least some similarity with sequences  
10 identified as AE000658 (Homo sapiens T-cell receptor alpha delta locus from bases 1 to 250529 (section 1 of 5) of the Complete Nucleotide Sequence), AF004231 (Homo sapiens monocyte/macrophage Ig-related receptor MIR-10 (MIR cl-10) mRNA, complete cds), G35352 (STS h14a108 5), H54023 (yq88h01.s1 Homo sapiens cDNA), H54181 (yq88h01.r1 Homo sapiens cDNA clone 202897 5'), T18551 (Human polycystic kidney disease normal  
15 PKD1 gene), and Z82206 (Human DNA sequence \*\*\* SEQUENCING IN PROGRESS \*\*\* from clone 370M22; HTGS phase 1). The predicted amino acid sequence disclosed herein for ij226\_6 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted ij226\_6 protein demonstrated at least some similarity to sequences identified as M22334 (unknown protein [Homo  
20 sapiens]). Based upon sequence similarity, ij226\_6 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two potential transmembrane domains within the ij226\_6 protein sequence centered around amino acids 37 and 62 of SEQ ID NO:114. The nucleotide sequence of ij226\_6 indicates that it may contain one or more of the following repetitive elements: L1, Alu, SVA.

25

#### Clone "nf443\_1"

A polynucleotide of the present invention has been identified as clone "nf443\_1". nf443\_1 was isolated from a human adult brain (substantia nigra) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No.  
30 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nf443\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nf443\_1 protein").

The nucleotide sequence of nf443\_1 as presently determined is reported in SEQ ID NO:115, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nf443\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:116.

5 Amino acids 21 to 43 of SEQ ID NO:116 are a possible leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 44. Due to the hydrophobic nature of this possible leader/signal sequence, it is likely to act as a transmembrane domain should the leader/signal sequence not be separated from the remainder of the nf443\_1 protein.

10 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nf443\_1 should be approximately 3800 bp.

The nucleotide sequence disclosed herein for nf443\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nf443\_1 demonstrated at least some similarity with sequences  
15 identified as AA417092 (zu07a12.s1 Soares testis NHT Homo sapiens cDNA clone 731134 3'), AA421511 (zu07a12.r1 Soares testis NHT Homo sapiens cDNA clone 731134 5'), T23707 (Human gene signature HUMGS05583), and U61233 (Bos taurus tubulin-folding cofactor D mRNA, complete cds). The predicted amino acid sequence disclosed herein for nf443\_1 was searched against the GenPept and GeneSeq amino acid sequence  
20 databases using the BLASTX search protocol. The predicted nf443\_1 protein demonstrated at least some similarity to sequences identified as U61233 (cofactor D [Bos taurus]). Based upon sequence similarity, nf443\_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of nf443\_1 indicates that it may contain an Alu repetitive element.

25 nf443\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 10 kDa was detected in conditioned medium fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "nt429\_1"

30 A polynucleotide of the present invention has been identified as clone "nt429\_1". nt429\_1 was isolated from a human adult brain (corpus callosum) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis

of computer analysis of the amino acid sequence of the encoded protein. nt429\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nt429\_1 protein").

The nucleotide sequence of nt429\_1 as presently determined is reported in SEQ ID NO:117, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nt429\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:118. Another possible reading frame and predicted amino acid sequence, encoded by base pairs 399 to 731 of nt429\_1 SEQ ID NO:117, is reported in SEQ ID NO:277; the amino acid sequence of SEQ ID NO:277 is hydrophobic in nature near its carboxyl terminus. The overlapping open reading frames corresponding to SEQ ID NO:118 and SEQ ID NO:277 could be joined if a frameshift were introduced into the nucleotide sequence of SEQ ID NO:117.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nt429\_1 should be approximately 1800 bp.

The nucleotide sequence disclosed herein for nt429\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. No significant hits were found in the database. The nucleotide sequence of nt429\_1 indicates that it may contain one or more of the following repetitive elements: Alu, SVA, A.

#### Clone "pe503\_1"

A polynucleotide of the present invention has been identified as clone "pe503\_1". pe503\_1 was isolated from a human adult blood (chronic myelogenous leukemia K5) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pe503\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pe503\_1 protein").

The nucleotide sequence of pe503\_1 as presently determined is reported in SEQ ID NO:119, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pe503\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:120.



Amino acids 79 to 91 of SEQ ID NO:120 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 92. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated  
5 from the remainder of the pe503\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pe503\_1 should be approximately 1300 bp.

The nucleotide sequence disclosed herein for pe503\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
10 FASTA search protocols. pe503\_1 demonstrated at least some similarity with sequences identified as AA298572 (EST114204 HSC172 cells I Homo sapiens cDNA 5' end), AA595242 (no33a12.s1 NCI\_CGAP\_Pr23 Homo sapiens cDNA clone IMAGE:1102462), H60941 (yr14g06.r1 Homo sapiens cDNA clone 205306 5'), H75686 (yr77g08.r1 Homo sapiens cDNA clone 2113585'), and R61206 (yh06d11.r1 Homo sapiens cDNA clone 42649  
15 5'). Based upon sequence similarity, pe503\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts four potential transmembrane domains within the pe503\_1 protein sequence centered around amino acids 50, 84, 107, and 148 of SEQ ID NO:120, respectively.

pe503\_1 protein was expressed in a COS cell expression system, and an expressed  
20 protein band of approximately 19 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "pe834\_6"

A polynucleotide of the present invention has been identified as clone "pe834\_6".  
25 pe834\_6 was isolated from a human adult blood (chronic myelogenous leukemia K5) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pe834\_6 is a full-length clone, including the entire coding sequence of a secreted  
30 protein (also referred to herein as "pe834\_6 protein").

The nucleotide sequence of pe834\_6 as presently determined is reported in SEQ ID NO:121, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pe834\_6 protein

corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:122. Another possible reading frame and predicted amino acid sequence, encoded by base pairs 414 to 725 of pe834\_6 SEQ ID NO:121, is reported in SEQ ID NO:278; the amino acid sequence of SEQ ID NO:278 is hydrophobic in nature near its carboxyl terminus. The overlapping open reading frames corresponding to SEQ ID NO:122 and SEQ ID NO:278 could be joined if a frameshift were introduced into the nucleotide sequence of SEQ ID NO:121.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pe834\_6 should be approximately 1300 bp.

The nucleotide sequence disclosed herein for pe834\_6 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pe834\_6 demonstrated at least some similarity with sequences identified as AA054341 (zl68f04.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 509791 3'), N21462 (yx57c10.s1 Homo sapiens cDNA clone 265842 3'), N34010 (yx75g07.r1 Homo sapiens cDNA clone 267612 5'), and T90232 (ye15c09.r1 Homo sapiens cDNA clone 117808 5'). Based upon sequence similarity, pe834\_6 proteins and each similar protein or peptide may share at least some activity.

pe834\_6 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 17 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "ya10\_1"

A polynucleotide of the present invention has been identified as clone "ya10\_1". ya10\_1 was isolated from a human adult testes cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ya10\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ya10\_1 protein").

The nucleotide sequence of ya10\_1 as presently determined is reported in SEQ ID NO:123, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ya10\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:124. Amino acids 6 to 18 of SEQ ID NO:124 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 19. Due to the

hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the ya10\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing  
5 clone ya10\_1 should be approximately 800 bp.

The nucleotide sequence disclosed herein for ya10\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. No clearly significant hits were found in these databases. BLASTX analysis of the ya10\_1 protein sequence revealed some amino acid sequence  
10 similarity to cystatins (cysteine protease inhibitors) of various species. Based upon this sequence similarity, ya10\_1 proteins and each similar protein or peptide may share at least some activity.

#### Clone "yb40\_1"

15 A polynucleotide of the present invention has been identified as clone "yb40\_1". yb40\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yb40\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yb40\_1 protein").

20 The nucleotide sequence of yb40\_1 as presently determined is reported in SEQ ID NO:125, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the yb40\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:126. Amino acids 29 to 41 of SEQ ID NO:126 are a possible leader/signal sequence, with the  
25 predicted mature amino acid sequence beginning at amino acid 42. Due to the hydrophobic nature of this possible leader/signal sequence, it could act as a transmembrane domain should it not be separated from the remainder of the yb40\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing  
30 clone yb40\_1 should be approximately 1700 bp.

The nucleotide sequence disclosed herein for yb40\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. yb40\_1 demonstrated at least some similarity with sequences

identified as AA595189 (no32f03.s1 NCI\_CGAP\_Pr23 Homo sapiens cDNA clone IMAGE:1102397), R74575 (yi58d04.r1 Homo sapiens cDNA clone 143431 5'), and T25773 (Human gene signature HUMGS08001). Based upon sequence similarity, yb40\_1 proteins and each similar protein or peptide may share at least some activity.

5

Clone "cs756\_2"

A polynucleotide of the present invention has been identified as clone "cs756\_2". cs756\_2 was isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was  
10 identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. cs756\_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "cs756\_2 protein").

The nucleotide sequence of cs756\_2 as presently determined is reported in SEQ ID  
15 NO:127, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the cs756\_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:128. Amino acids 211 to 223 of SEQ ID NO:128 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 224. Due to the  
20 hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the cs756\_2 protein. The TopPredII computer program predicts a potential transmembrane domain within the cs756\_2 protein sequence of SEQ ID NO:128, centered around amino acid 15 of SEQ ID NO:128; amino acids 2 to 14 of SEQ ID NO:128  
25 are also a possible leader/signal sequence, with the predicted mature amino acid sequence in that case beginning at amino acid 15.

Another possible cs756\_2 reading frame and predicted amino acid sequence, encoded by base pairs 385 to 825 of SEQ ID NO:127, is reported in SEQ ID NO:279; the TopPredII computer program predicts a potential transmembrane domain centered  
30 around amino acid 100 of SEQ ID NO:279. The open reading frames corresponding to SEQ ID NO:279 and SEQ ID NO:128 could be joined if a frameshift were introduced into the nucleotide sequence of SEQ ID NO:127.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone cs756\_2 should be approximately 3000 bp.

The nucleotide sequence disclosed herein for cs756\_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. cs756\_2 demonstrated at least some similarity with sequences identified as AA398077 (zt58c03.s1 Soares testis NHT Homo sapiens cDNA clone 726532 3'), AA541286 (nf97e03.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA clone IMAGE:927868), W28620 (49c2 Human retina cDNA randomly primed sublibrary Homo sapiens cDNA), and W47601 (zc35g08.r1 Soares senescent fibroblasts NbHSF Homo sapiens cDNA clone 324350 5'). The predicted amino acid sequence disclosed herein for SEQ ID NO:279 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted SEQ ID NO:279 protein demonstrated at least some similarity to sequences identified as L76938 (Werner syndrome gene, complete cds [Homo sapiens]). "Werner's syndrome (WS) is an inherited disease with clinical symptoms resembling premature aging ... [the] predicted protein is 1432 amino acids in length and shows significant similarity to DNA helicases" (Yu *et al.*, 1996, *Science* 272(5259):258-262, which is incorporated by reference herein). Based upon sequence similarity, cs756\_2 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of cs756\_2 indicates that it may contain one or more of the following repetitive elements: MIR, MER.

#### Clone "ew150\_1"

A polynucleotide of the present invention has been identified as clone "ew150\_1". ew150\_1 was isolated from a human adult placenta cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ew150\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ew150\_1 protein").

The nucleotide sequence of ew150\_1 as presently determined is reported in SEQ ID NO:129, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ew150\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:130.

Amino acids 26 to 38 of SEQ ID NO:130 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 39. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated  
5 from the remainder of the ew150\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ew150\_1 should be approximately 2000 bp.

The nucleotide sequence disclosed herein for ew150\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
10 FASTA search protocols. ew150\_1 demonstrated at least some similarity with sequences identified as AA563938 (nk23b12.s1 NCI\_CGAP\_Col1 Homo sapiens cDNA clone IMAGE 1014335), D63209 (Human placenta cDNA 5'-end GEN-506F01), M90423 (Bacteriophage US3 lytic-enzyme), W23461 (zb33c01.r1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 305376 5'), and Z56916 (H.sapiens CpG DNA, clone 153b7,  
15 forward read cpg153b7.ft1a). In the region around position 1514 of SEQ ID NO:129, ew150\_1 also demonstrated at least some similarity with sequences encoding a mitochondrial energy-transfer proteins signature motif which is found in mitochondrial and other membrane proteins. Based upon sequence similarity, ew150\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer  
20 program predicts ten potential transmembrane domains within the ew150\_1 protein sequence, which are centered around amino acids 70, 106, 133, 200, 314, 349, 387, 457, 504, and 527 of SEQ ID NO:130, respectively.

#### Clone "gg894\_13"

25 A polynucleotide of the present invention has been identified as clone "gg894\_13". gg894\_13 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. gg894\_13 is a full-length  
30 clone, including the entire coding sequence of a secreted protein (also referred to herein as "gg894\_13 protein").

The nucleotide sequence of gg894\_13 as presently determined is reported in SEQ ID NO:131, and includes a poly(A) tail. What applicants presently believe to be the

proper reading frame and the predicted amino acid sequence of the gg894\_13 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:132. Amino acids 41 to 53 of SEQ ID NO:132 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 54. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the gg894\_13 protein. Another possible gg894\_13 reading frame and predicted amino acid sequence, encoded by base pairs 602 to 1129 of SEQ ID NO:131, is reported in SEQ ID NO:280. The open reading frames corresponding to SEQ ID NO:280 and SEQ ID NO:132 could be joined if a frameshift were introduced into the nucleotide sequence of SEQ ID NO:131.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone gg894\_13 should be approximately 2400 bp.

The nucleotide sequence disclosed herein for gg894\_13 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. gg894\_13 demonstrated at least some similarity with sequences identified as H57424 (yr13a10.s1 Homo sapiens cDNA clone 205146 3'), T23885 (Human gene signature HUMGS05820), and W80358 (zh49a07.s1 Soares fetal liver spleen 1NFLS S1 Homo sapiens cDNA clone 415380 3'). Based upon sequence similarity, gg894\_13 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the gg894\_13 protein sequence centered around amino acid 115 of SEQ ID NO:132. The nucleotide sequence of gg894\_13 indicates that it may contain a RBMI repetitive element.

#### Clone "it217\_2"

A polynucleotide of the present invention has been identified as clone "it217\_2". it217\_2 was isolated from a human adult brain (thalamus) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. it217\_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "it217\_2 protein").

The nucleotide sequence of it217\_2 as presently determined is reported in SEQ ID NO:133, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the it217\_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:134.

5 Another possible it217\_2 reading frame and predicted amino acid sequence, encoded by base pairs 45 to 311 of SEQ ID NO:133, is reported in SEQ ID NO:281. Amino acids 36 to 48 of SEQ ID NO:281 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 49. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should

10 the predicted leader/signal sequence not be separated from the remainder of the it217\_2 protein. The open reading frames corresponding to SEQ ID NO:281 and SEQ ID NO:134 could be joined if at least one frameshift were introduced into the nucleotide sequence of SEQ ID NO:133.

The EcoRI/NotI restriction fragment obtainable from the deposit containing

15 clone it217\_2 should be approximately 2250 bp.

The nucleotide sequence disclosed herein for it217\_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. it217\_2 demonstrated at least some similarity with sequences identified as AA242969 (zr65h09.r1 Soares NhHMPu S1 Homo sapiens cDNA clone

20 668321 5' similar to SW SCC2\_HUMAN P48594 SQUAMOUS CELL CARCINOMA ANTIGEN 2 ;contains Alu repetitive element), B44876 (HS-1060-A1-G06-MR.abi CIT Human Genomic Sperm Library C Homo sapien genomic clone Plate CT 782 Col 11 Row M), H82168 (yv78d08.r1 Homo sapiens cDNA clone), S66896 (squamous cell carcinoma antigen), U19556 (Human squamous cell carcinoma antigen 1 (SCCA1) mRNA, complete

25 cds), U19557 (Human squamous cell carcinoma antigen 2 (SCCA2) mRNA, complete cds), and U35459 (Human bomapin mRNA, complete cds). The predicted amino acid sequence disclosed herein for it217\_2 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted it217\_2 protein demonstrated at least some similarity to sequences identified as L40377 (cytoplasmic

30 antiproteinase 2 [Homo sapiens]), M34352 (ovalbumin [Gallus gallus]), M91161 (serpin [Equus caballus]), R25276 (SCC antigen), R48379 (Human megakaryocyte differentiation factor), S66896 (squamous cell carcinoma antigen, SCC antigen serine protease inhibitor [human, Peptide, 390 aa] [Homo sapiens]), U19568 (squamous cell carcinoma antigen



[Homo sapiens]), and U19576 (squamous cell carcinoma antigen [Homo sapiens]). Human bomapin may play a role in the regulation of protease activities during hematopoiesis (Riewald *et al.*, 1995, *J. Biol. Chem.* 270: 26754, which is incorporated by reference herein). Serpins are SERine Proteinase INhibitors and are considered  
5 extracellular in localization. Human squamous cell carcinoma antigen (SSCA) is a member of the serpin family of proteinase inhibitors, purified from sera of cancer patients. Based upon sequence similarity, it217\_2 proteins and each similar protein or peptide may share at least some activity.

10        Clone "ml235\_2"

A polynucleotide of the present invention has been identified as clone "ml235\_2". ml235\_2 was isolated from a human adult brain (caudate nucleus) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis  
15 of computer analysis of the amino acid sequence of the encoded protein. ml235\_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ml235\_2 protein").

The nucleotide sequence of ml235\_2 as presently determined is reported in SEQ ID NO:135, and includes a poly(A) tail. What applicants presently believe to be the  
20 proper reading frame and the predicted amino acid sequence of the ml235\_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:136. Amino acids 3 to 15 of SEQ ID NO:136 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 16. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a  
25 transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the ml235\_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ml235\_2 should be approximately 1400 bp.

The nucleotide sequence disclosed herein for ml235\_2 was searched against the  
30 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ml235\_2 demonstrated at least some similarity with sequences identified as AA160887 (zo79b05.s1 Stratagene pancreas (#937208) Homo sapiens cDNA clone 593073 3'), R14349 (yf79f12.r1 Homo sapiens cDNA clone 28451 5'), and R54256

(yg74f07.r1 Homo sapiens cDNA clone 39059 5'). Based upon sequence similarity, ml235\_2 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the ml235\_2 protein sequence centered around amino acid 25 of SEQ ID NO:136.

5

Clone "mt24\_2"

A polynucleotide of the present invention has been identified as clone "mt24\_2". mt24\_2 was isolated from a human adult testes cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was  
10 identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. mt24\_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "mt24\_2 protein").

The nucleotide sequence of mt24\_2 as presently determined is reported in SEQ ID  
15 NO:137, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the mt24\_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:138. Amino acids 30 to 42 of SEQ ID NO:138 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 43. Due to the  
20 hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the mt24\_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone mt24\_2 should be approximately 1400 bp.

25 The nucleotide sequence disclosed herein for mt24\_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. mt24\_2 demonstrated at least some similarity with sequences identified as AA062589 (zf68f04.r1 Soares pineal gland N3HPG Homo sapiens cDNA clone 382111 5') and T19332 (b08016t Testis 1 Homo sapiens cDNA clone b08016 5' end).  
30 Based upon sequence similarity, mt24\_2 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts four potential transmembrane domains within the mt24\_2 protein sequence centered around amino acids 38, 153, 167, and 232 of SEQ ID NO:138, respectively.

Clone "pe584\_2"

A polynucleotide of the present invention has been identified as clone "pe584\_2". pe584\_2 was isolated from a human adult blood (chronic myelogenous leukemia K5) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pe584\_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pe584\_2 protein").

The nucleotide sequence of pe584\_2 as presently determined is reported in SEQ ID NO:139, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pe584\_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:140. Amino acids 27 to 39 of SEQ ID NO:140 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 40. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the pe584\_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pe584\_2 should be approximately 3000 bp.

The nucleotide sequence disclosed herein for pe584\_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pe584\_2 demonstrated at least some similarity with sequences identified as AA303149 (EST13039 Uterus tumor I), AA405004 (zt06e03.s1 NCI\_CGAP\_GCB1 Homo sapiens cDNA clone IMAGE 712348 3'), AA481230 (aa34g01.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA clone 815184 5' similar to SW TCR2\_ECOLI P02981 TETRACYCLINE RESISTANCE PROTEIN), D88315 (Mouse mRNA for tetracycline transporter-like protein, complete cds), and T10077 (seq1295 Homo sapiens cDNA clone b4HB3MA-COT8-HAP-Ft109 5'). The predicted amino acid sequence disclosed herein for pe584\_2 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted pe584\_2 protein demonstrated at least some similarity to sequences identified as D88315 (tetracycline transporter-like protein [Mus musculus]). Mouse tetracycline transporter-like protein is a sugar transporter (Matsuo *et al.*, 1997, *Biochem. Biophys. Res. Comm.* 238: 126-192, which

is incorporated by reference herein). Based upon sequence similarity, pe584\_2 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts eleven potential transmembrane domains within the pe584\_2 protein sequence, which are centered around amino acids 32, 55, 78, 114, 142, 196, 235, 264, 287, 332, and 375 of SEQ ID NO:140, respectively.

#### Clone "pj323\_2"

A polynucleotide of the present invention has been identified as clone "pj323\_2". pj323\_2 was isolated from a human fetal carcinoma (NTD2 cells treated with retinoic acid for 23 days) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pj323\_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pj323\_2 protein").

The nucleotide sequence of pj323\_2 as presently determined is reported in SEQ ID NO:141, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pj323\_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:142. Amino acids 150 to 162 of SEQ ID NO:142 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 163. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the pj323\_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pj323\_2 should be approximately 2500 bp.

The nucleotide sequence disclosed herein for pj323\_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pj323\_2 demonstrated at least some similarity with sequences identified as AA160454 (zo74g05.r1 Stratagene pancreas (#937208) Homo sapiens cDNA clone 592664 5'), AA398257 (zt60a08.s1 Soares testis NHT Homo sapiens cDNA clone 726710 3'), and T47284 (yb64g11.s1 Homo sapiens cDNA clone 76004 3'). The predicted amino acid sequence disclosed herein for pj323\_2 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The

predicted pj323\_2 protein demonstrated at least some similarity to human integral nuclear envelope protein, lamin B receptors from several species, and sterol reductases from several species. Lamin B receptors have hydrophobic carboxy terminal portions and hydrophilic amino terminal portions. Antibodies to lamin B receptors have been found  
5 in patients with primary biliary cirrhosis. Sterol reductases demonstrate sequence similarity to the hydrophobic portions of lamin B receptors. Based upon sequence similarity, pj323\_2 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts six potential transmembrane domains within the pj323\_2 protein sequence, which are centered around amino acids 47,  
10 106, 164, 187, 341, and 432 of SEQ ID NO:142, respectively.

pj323\_2 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 46 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

15        Clone "yb24\_1"

A polynucleotide of the present invention has been identified as clone "yb24\_1". yb24\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yb24\_1 is a full-length clone, including the  
20 entire coding sequence of a secreted protein (also referred to herein as "yb24\_1 protein").

The nucleotide sequence of yb24\_1 as presently determined is reported in SEQ ID NO:143, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the yb24\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:144.  
25 Amino acids 25 to 37 of SEQ ID NO:144 are a predicted leader/signal sequence with the

FASTA search protocols. yb24\_1 demonstrated at least some similarity with sequences identified as AA149807 (z147c09.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 505072 3') and AB003515 (Rat mRNA for GEF-2, complete cds). Based upon sequence similarity, yb24\_1 proteins and each similar protein or peptide may share at least some activity.

#### Clone "yb44\_1"

A polynucleotide of the present invention has been identified as clone "yb44\_1". yb44\_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yb44\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yb44\_1 protein").

The nucleotide sequence of yb44\_1 as presently determined is reported in SEQ ID NO:145, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the yb44\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:146. Amino acids 10 to 22 of SEQ ID NO:146 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 23. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the yb44\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone yb44\_1 should be approximately 2000 bp.

The nucleotide sequence disclosed herein for yb44\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. yb44\_1 demonstrated at least some similarity with sequences identified as AC000016 (\*\* SEQUENCING IN PROGRESS \*\* EPM1/APECED region of chromosome 21, BAC clone B4P3; HTGS phase 1, 10 unordered pieces). The predicted amino acid sequence disclosed herein for yb44\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted yb44\_1 protein demonstrated at least some similarity to sequences identified as R72377 (Human auxillary cytochrome P450 species 2D6 variant 2 protein) and U44753 (cytochrome P450 [Drosophila melanogaster]). Based upon sequence similarity, yb44\_1

proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts three additional potential transmembrane domains within the yb44\_1 protein sequence, which are centered around amino acids 82, 128, and 361 of SEQ ID NO:146, respectively. The nucleotide sequence of yb44\_1 indicates that it  
5 may contain one or more of the following repetitive elements: Alu, AT, TATACA, MER44A, TACA.

Clone "bn69\_15"

A polynucleotide of the present invention has been identified as clone "bn69\_15".  
10 bn69\_15 was isolated from a human adult placenta cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bn69\_15 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein  
15 as "bn69\_15 protein").

The nucleotide sequence of bn69\_15 as presently determined is reported in SEQ ID NO:147, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bn69\_15 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:148.  
20 Amino acids 47 to 59 of SEQ ID NO:148 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 60. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the bn69\_15 protein. Another potential bn69\_15 reading frame and  
25 predicted amino acid sequence is encoded by basepairs 1008 to 1352 of SEQ ID NO:147 and is reported in SEQ ID NO:282.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bn69\_15 should be approximately 2800 bp.

The nucleotide sequence disclosed herein for bn69\_15 was searched against the  
30 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bn69\_15 demonstrated at least some similarity with sequences identified as H80692 (yv01b10.r1 Homo sapiens cDNA clone 241435 5'), T64701 (yc48d02.r1 Homo sapiens cDNA clone 83907 5'), and W21368 (zb59c01.r1 Soares fetal

lung NbHL19W Homo sapiens cDNA clone 307872 5' similar to gb:M83186 CYTOCHROME C OXIDASE POLYPEPTIDE VIIA-HEART PRECURSOR (HUMAN)). Based upon sequence similarity, bn69\_15 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional  
5 potential transmembrane domain within the bn69\_15 protein sequence centered around amino acid 32 of SEQ ID NO:148.

Clone "cb110\_1"

A polynucleotide of the present invention has been identified as clone "cb110\_1".  
10 cb110\_1 was isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. cb110\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as  
15 "cb110\_1 protein").

The nucleotide sequence of cb110\_1 as presently determined is reported in SEQ ID NO:149, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the cb110\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:150.  
20 Amino acids 36 to 48 of SEQ ID NO:150 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 49. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the cb110\_1 protein.

25 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone cb110\_1 should be approximately 900 bp.

The nucleotide sequence disclosed herein for cb110\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. cb110\_1 demonstrated at least some similarity with sequences  
30 identified as AC001083 (Homo sapiens (subclone 2\_a6 from BAC H75) DNA sequence, complete sequence), D28485 (Human MSMB gene for beta-microseminoprotein (MSP), promoter region and exon1), and Z98052 (Human DNA sequence \*\*\* SEQUENCING IN



PROGRESS \*\*\* from clone 505B13; HTGS phase 1). Based upon sequence similarity, cb110\_1 proteins and each similar protein or peptide may share at least some activity.

Clone "ch4\_11"

5 A polynucleotide of the present invention has been identified as clone "ch4\_11". ch4\_11 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ch4\_11 is a full-length clone,  
10 including the entire coding sequence of a secreted protein (also referred to herein as "ch4\_11 protein").

The nucleotide sequence of ch4\_11 as presently determined is reported in SEQ ID NO:151, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ch4\_11 protein  
15 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:152. Amino acids 21 to 33 of SEQ ID NO:152 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 34. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated  
20 from the remainder of the ch4\_11 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ch4\_11 should be approximately 1600 bp.

The nucleotide sequence disclosed herein for ch4\_11 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
25 FASTA search protocols. ch4\_11 demonstrated at least some similarity with sequences identified as AA318160 (EST20431 Retina II Homo sapiens cDNA 5' end), R94133 (yt74g06.r1 Soares fetal liver spleen 1NFLS Homo sapiens cDNA clone 276275 5'), and W27798 (37h1 Human retina cDNA randomly primed sublibrary Homo sapiens). The predicted amino acid sequence disclosed herein for ch4\_11 was searched against the  
30 GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted ch4\_11 protein demonstrated at least some similarity to sequences identified as L28819 (involucrin [Mus musculus]). The ch4\_11 protein is the human homologue of the mouse K483\_1 protein (see GenBank I80067 and I80068, GeneSeq

V09119, V09120, and W42028, and U.S. Patent No. 5,708,157). Based upon sequence similarity, ch4\_11 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts three potential transmembrane domains within the ch4\_11 protein sequence centered around amino acids 28, 189, and 280 of SEQ ID NO:152, respectively.

Clone "cn621\_8"

A polynucleotide of the present invention has been identified as clone "cn621\_8". cn621\_8 was isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. cn621\_8 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "cn621\_8 protein").

The nucleotide sequence of cn621\_8 as presently determined is reported in SEQ ID NO:153, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the cn621\_8 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:154.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone cn621\_8 should be approximately 3500 bp.

The nucleotide sequence disclosed herein for cn621\_8 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. cn621\_8 demonstrated at least some similarity with sequences identified as W18181 (IMAGE:20099 Soares infant brain 1N1B Homo sapiens cDNA clone 20099), W60570 (zd26g04.r1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 3418145'), W60661 (zd26g04.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone), and Z84474 (Human DNA sequence from PAC 111M5 on chromosome 6. Contains BBC1, RFP finger protein, EST, STS, tRNAs and polymorphic repeat). The predicted amino acid sequence disclosed herein for cn621\_8 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted cn621\_8 protein demonstrated at least some similarity to sequences identified as L35279 (BMP-1 [Homo sapiens]), U91963 (tollid-like (TLL) [Homo sapiens]), and X64414 (low density lipoprotein receptor [Mus musculus]). Based upon sequence similarity, cn621\_8 proteins

and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the cn621\_8 protein sequence centered around amino acid 220 of SEQ ID NO:154.

5        Clone "gy621\_1"

A polynucleotide of the present invention has been identified as clone "gy621\_1". gy621\_1 was isolated from a human adult testes cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer  
10    analysis of the amino acid sequence of the encoded protein. gy621\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "gy621\_1 protein").

The nucleotide sequence of gy621\_1 as presently determined is reported in SEQ ID NO:155, and includes a poly(A) tail. What applicants presently believe to be the  
15    proper reading frame and the predicted amino acid sequence of the gy621\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:156. Amino acids 11 to 23 of SEQ ID NO:156 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 24. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a  
20    transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the gy621\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone gy621\_1 should be approximately 3800 bp.

The nucleotide sequence disclosed herein for gy621\_1 was searched against the  
25    GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. gy621\_1 demonstrated at least some similarity with sequences identified as AA166536 (ms63h05.r1 Stratagene mouse embryonic carcinoma (#937317) Mus musculus cDNA clone 616281 5'), AA416723 (zu08a04.s1 Soares testis NHTT Homo sapiens cDNA clone 731214 3'), and AA463756 (aa07a05.r1 Soares NhHMPu S1 Homo  
30    sapiens cDNA clone 812528 5'). Based upon sequence similarity, gy621\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts at least one additional potential transmembrane domains within the

gy621\_1 protein sequence of SEQ ID NO:156. The nucleotide sequence of gy621\_1 indicates that it may contain one or more AC1 or AC2 repetitive elements.

Clone "hb1041\_2"

5 A polynucleotide of the present invention has been identified as clone "hb1041\_2". hb1041\_2 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. hb1041\_2 is a full-length  
10 clone, including the entire coding sequence of a secreted protein (also referred to herein as "hb1041\_2 protein").

The nucleotide sequence of hb1041\_2 as presently determined is reported in SEQ ID NO:157, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the hb1041\_2 protein  
15 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:158. Amino acids 55 to 67 of SEQ ID NO:158 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 68. Due to the hydrophobic nature of the predicted leader/signal sequence, it may act as a transmembrane domain should the predicted leader/signal sequence not be separated  
20 from the remainder of the hb1041\_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone hb1041\_2 should be approximately 2450 bp.

The nucleotide sequence disclosed herein for hb1041\_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
25 FASTA search protocols. hb1041\_2 demonstrated at least some similarity with sequences identified as AA050445 (mj21c12.r1 Soares mouse embryo NbME13.5 14.5 Mus musculus cDNA clone 476758 5'), AA087161 (mo11b05.r1 Life Tech mouse embryo 105dpc 10665016 Mus musculus cDNA clone 553233 5'), and W84558 (zd89h10.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 356707 3'). The predicted amino acid sequence  
30 disclosed herein for hb1041\_2 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted hb1041\_2 protein demonstrated at least some similarity to sequences identified as AB000459 (unnamed

protein product [Homo sapiens]). Based upon sequence similarity, hb1041\_2 proteins and each similar protein or peptide may share at least some activity.

Clone "mh703\_1"

5 A polynucleotide of the present invention has been identified as clone "mh703\_1". mh703\_1 was isolated from a human adult brain (thalamus) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. mh703\_1 is a full-  
10 length clone, including the entire coding sequence of a secreted protein (also referred to herein as "mh703\_1 protein").

The nucleotide sequence of mh703\_1 as presently determined is reported in SEQ ID NO:159, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the mh703\_1 protein  
15 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:160.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone mh703\_1 should be approximately 1700 bp.

The nucleotide sequence disclosed herein for mh703\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
20 FASTA search protocols. mh703\_1 demonstrated at least some similarity with sequences identified as AA173536 (zp04e07.r1 Stratagene ovarian cancer (#937219) Homo sapiens cDNA clone 595428 5'), AA173577 (zp04e07.s1 Stratagene ovarian cancer (#937219) Homo sapiens cDNA clone 595428 3'), AA278788 (zs79a09.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA clone IMAGE 703672 5' similar to TR E189399 E189399 HYPOTHETICAL 51.4 KD  
25 PROTEIN), and T26646 (Human gene signature HUMGS08893). The predicted amino acid sequence disclosed herein for mh703\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted mh703\_1 protein demonstrated at least some similarity to sequences identified as R85881 (WD-40 domain-contg. YCW2 protein) and U80447 (similar to the beta  
30 transducin family [Caenorhabditis elegans]). mh703\_1 protein contains at least two beta-transducin family Trp-Asp repeat signature motifs, and also contains the WD-40 motif of G-proteins. Based upon sequence similarity, mh703\_1 proteins and each similar protein or peptide may share at least some activity.

mh703\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 51 kDa was detected in conditioned medium using SDS polyacrylamide gel electrophoresis.

5        Clone "na461\_19"

A polynucleotide of the present invention has been identified as clone "na461\_19". na461\_19 was isolated from a human adult brain (corpus callosum) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis  
10 of computer analysis of the amino acid sequence of the encoded protein. na461\_19 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "na461\_19 protein").

The nucleotide sequence of na461\_19 as presently determined is reported in SEQ ID NO:161, and includes a poly(A) tail. What applicants presently believe to be the  
15 proper reading frame and the predicted amino acid sequence of the na461\_19 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:162. Amino acids 63 to 75 of SEQ ID NO:162 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 76. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a  
20 transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the na461\_19 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone na461\_19 should be approximately 2300 bp.

The nucleotide sequence disclosed herein for na461\_19 was searched against the  
25 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. na461\_19 demonstrated at least some similarity with sequences identified as AA032203 (zf01d04.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 375655 3'), AA203707 (zx52c12.r1 Soares fetal liver spleen 1NFLS S1 Homo sapiens cDNA clone 446134 5' similar to contains element MER2 repetitive element), AA262333  
30 (zr70h11.s1 Soares NhHMPu S1 Homo sapiens cDNA clone 668805 3'), AA318276 (EST20340 Retina II Homo sapiens cDNA 5' end), AA436588 (zv08e12.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 753070 5'), and T21229 (Human gene signature

HUMGS02545). Based upon sequence similarity, na461\_19 proteins and each similar protein or peptide may share at least some activity.

Clone "na492\_2"

5 A polynucleotide of the present invention has been identified as clone "na492\_2". na492\_2 was isolated from a human adult brain (corpus callosum) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. na492\_2 is a full-  
10 length clone, including the entire coding sequence of a secreted protein (also referred to herein as "na492\_2 protein").

The nucleotide sequence of na492\_2 as presently determined is reported in SEQ ID NO:163, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the na492\_2 protein  
15 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:164. Amino acids 321 to 333 of SEQ ID NO:164 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 334. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated  
20 from the remainder of the na492\_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone na492\_2 should be approximately 1800 bp.

The nucleotide sequence disclosed herein for na492\_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
25 FASTA search protocols. na492\_2 demonstrated at least some similarity with sequences identified as AA514389 (nf57b05.s1 NCI\_CGAP\_Co3 Homo sapiens cDNA clone IMAGE:923985), H81154 (yu60f02.r1 Homo sapiens cDNA clone 230523 5'), and R89359 (yq05c05.s1 Homo sapiens cDNA clone 196040 3'). The predicted amino acid sequence disclosed herein for na492\_2 was searched against the GenPept and GeneSeq amino acid  
30 sequence databases using the BLASTX search protocol. The predicted na492\_2 protein demonstrated at least some similarity to sequences identified as AB004534 (pi015 [Schizosaccharomyces pombe]). Based upon sequence similarity, na492\_2 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer

program predicts two potential transmembrane domains within the na492\_2 protein sequence, one centered around amino acid 350 and another around amino acid 370 of SEQ ID NO:164.

5        Clone "na669\_10"

A polynucleotide of the present invention has been identified as clone "na669\_10". na669\_10 was isolated from a human adult brain (corpus callosum) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis  
10 of computer analysis of the amino acid sequence of the encoded protein. na669\_10 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "na669\_10 protein").

The nucleotide sequence of na669\_10 as presently determined is reported in SEQ ID NO:165, and includes a poly(A) tail. What applicants presently believe to be the  
15 proper reading frame and the predicted amino acid sequence of the na669\_10 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:166. Amino acids 40 to 52 of SEQ ID NO:166 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 53. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a  
20 transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the na669\_10 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone na669\_10 should be approximately 3300 bp.

The nucleotide sequence disclosed herein for na669\_10 was searched against the  
25 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. na669\_10 demonstrated at least some similarity with sequences identified as AA035207 (zk27h11.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 471813 3'), AA429797 (zw57d10.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 774163 5'), AA512946 (nh91d01.s1 NCI\_CGAP\_Br1.1 Homo sapiens cDNA  
30 clone IMAGE:965857), C20746 (HUMGS0004776, Human Gene Signature), and N33343 (yy08d08.s1 Homo sapiens cDNA clone 270639 3'). Based upon sequence similarity, na669\_10 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two potential transmembrane domains within



the na669\_10 protein sequence, one centered around amino acid 11 and another around amino acid 46 of SEQ ID NO:166.

Clone "co821\_31"

5 A polynucleotide of the present invention has been identified as clone "co821\_31". co821\_31 was isolated from a human adult brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. co821\_31 is a full-length  
10 clone, including the entire coding sequence of a secreted protein (also referred to herein as "co821\_31 protein").

The nucleotide sequence of co821\_31 as presently determined is reported in SEQ ID NO:167, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the co821\_31 protein  
15 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:168. Amino acids 87 to 99 of SEQ ID NO:168 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 100. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated  
20 from the remainder of the co821\_31 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone co821\_31 should be approximately 2400 bp.

The nucleotide sequence disclosed herein for co821\_31 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
25 FASTA search protocols. co821\_31 demonstrated at least some similarity with sequences identified as AA488906 (aa55a02.r1 NCI\_CGAP\_GCB1 Homo sapiens cDNA clone IMAGE:8248105' similar to TR:G607003 G607003 BETA TRANSDUCIN-LIKE PROTEIN), L26690 (Mus musculus expressed sequence tag EST F101), N30002 (yx82e02.s1 Homo sapiens cDNA clone 268250 3'), R82926 (EST23j22 Clontech adult human fat cell library  
30 HL1108A Homo sapiens cDNA clone 23j22), T20673 (Human gene signature HUMGS01889), and W44749 (zb98b11.s1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 320829 3'). The predicted amino acid sequence disclosed herein for co821\_31 was searched against the GenPept and GeneSeq amino acid sequence databases

using the BLASTX search protocol. The predicted co821\_31 protein demonstrated at least some similarity to sequences identified as U51030 (Ydr267cp [Saccharomyces cerevisiae]). The predicted co821\_31 protein also demonstrated at least some similarity to U92792 (general transcriptional repressor Tup1 [Schizosaccharomyces pombe]), L28125 (beta transducin-like protein (het-e1) [Podospora anserina]), and other proteins containing WD-40 motifs. Based upon sequence similarity, co821\_31 proteins and each similar protein or peptide may share at least some activity.

#### Clone "dk329\_1"

10 A polynucleotide of the present invention has been identified as clone "dk329\_1". dk329\_1 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. dk329\_1 is a full-length  
15 clone, including the entire coding sequence of a secreted protein (also referred to herein as "dk329\_1 protein").

The nucleotide sequence of dk329\_1 as presently determined is reported in SEQ ID NO:169, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the dk329\_1 protein  
20 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:170. Amino acids 71 to 83 of SEQ ID NO:170 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 84. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated  
25 from the remainder of the dk329\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone dk329\_1 should be approximately 1300 bp.

The nucleotide sequence disclosed herein for dk329\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
30 FASTA search protocols. dk329\_1 demonstrated at least some similarity with sequences identified as AA147429 (zo39g07.r1 Stratagene endothelial cell 937223 Homo sapiens cDNA clone 589308 5' similar to WP T14G10.6 CE06452 LEUCOCYTE SURFACE ANTIGEN CD53 LINE), AA190572 (zp42h08.r1 Stratagene muscle 937209 Homo sapiens

cDNA clone 612159 5' similar to WP T14G10.6 CE06452 LEUCOCYTE SURFACE ANTIGEN CD53 LINE), AA234042 (zr51a05.s1 Soares NhHMPu S1 Homo sapiens cDNA clone 666896 3' similar to WP:T14G10.6 CE06452 LEUCOCYTE SURFACE ANTIGEN CD53 LINE), AA236262 (zr51a05.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 5 666896 5' similar to WP:T14G10.6 CE06452 LEUCOCYTE SURFACE ANTIGEN CD53 LINE), N72328 (yv31f12.r1 Homo sapiens cDNA clone 244367 5' similar to SW A15\_HUMAN P41732 CELL SURFACE GLYCOPROTEIN A15), and W50192 (mb08d07.r1 Life Tech mouse brain Mus musculus cDNA clone 319597 5' similar to SW:CD53\_HUMAN P19397 LEUCOCYTE SURFACE ANTIGEN CD53). The predicted 10 amino acid sequence disclosed herein for dk329\_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted dk329\_1 protein demonstrated at least some similarity to sequences identified as Z68880 (T14G10.6 [Caenorhabditis elegans]) and a variety of membrane proteins involved in immune function. Based upon sequence similarity, dk329\_1 proteins and 15 each similar protein or peptide may share at least some activity. The TopPredII computer program predicts three potential transmembrane domains within the dk329\_1 protein sequence, centered around amino acids 31, 71, and 103 of SEQ ID NO:170, respectively.

dk329\_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 18 kDa was detected in membrane fractions using SDS 20 polyacrylamide gel electrophoresis.

#### Clone "fx317\_11"

A polynucleotide of the present invention has been identified as clone "fx317\_11". fx317\_11 was isolated from a human fetal brain cDNA library using methods which are 25 selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. fx317\_11 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "fx317\_11 protein").

30 The nucleotide sequence of fx317\_11 as presently determined is reported in SEQ ID NO:171, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the fx317\_11 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:172.

Amino acids 229 to 241 of SEQ ID NO:172 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 242. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the fx317\_11 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone fx317\_11 should be approximately 1900 bp.

The nucleotide sequence disclosed herein for fx317\_11 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. fx317\_11 demonstrated at least some similarity with sequences identified as AA505600 (nh93h11.s1 NCI\_CGAP\_Br2 Homo sapiens cDNA clone IMAGE:966117), N47450 (yy89c09.r1 Homo sapiens cDNA clone 280720 5' similar to contains element PTR5 repetitive element), T64549 (Human activated platelet protein-2 APP-2 cDNA), and W52611 (zc49e02.r1 Soares senescent fibroblasts NbHSF Homo sapiens cDNA clone 325658 5'). The predicted amino acid sequence disclosed herein for fx317\_11 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted fx317\_11 protein demonstrated at least some similarity to sequences identified as W15413 (Human activated platelet protein-2 APP-2) and W15414 (Human activated platelet protein-2 APP-2 alternatively spliced variant). APP-2 protein is expressed on activated human platelets. Based upon sequence similarity, fx317\_11 proteins and each similar protein or peptide may share at least some activity.

#### Clone "lp547\_4"

A polynucleotide of the present invention has been identified as clone "lp547\_4". lp547\_4 was isolated from a human adult blood (peripheral blood mononuclear cells treated *in vivo* with granulocyte-colony stimulating factor) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. lp547\_4 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "lp547\_4 protein").

The nucleotide sequence of lp547\_4 as presently determined is reported in SEQ ID NO:173, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the lp547\_4 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:174.

5 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone lp547\_4 should be approximately 1800 bp.

The nucleotide sequence disclosed herein for lp547\_4 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. lp547\_4 demonstrated at least some similarity with sequences  
10 identified as AA442560 (zv75g07.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 7595165' similar to TR:G436941 G436941 PHORBOLINI). The predicted amino acid sequence disclosed herein for lp547\_4 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted lp547\_4 protein demonstrated at least some similarity to sequences identified as R58704 (Apo-B  
15 RNA editing protein), U03891 (phorbolin I [Homo sapiens]), and U21951 (apolipoprotein B mRNA-editing component 1 [Mus musculus]). U03891 protein (phorbolin I) is upregulated in psoriatic keratinocytes. The predicted lp547\_4 protein also contains a cytidine and deoxycytidylate deaminases zinc-binding region signature. Based upon sequence similarity, lp547\_4 proteins and each similar protein or peptide may share at  
20 least some activity. The TopPredII computer program predicts a potential transmembrane domain within the lp547\_4 protein sequence, centered around amino acid 290 of SEQ ID NO:174; amino acids 278 to 290 are also a possible leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 291.

lp547\_4 protein was expressed in a COS cell expression system, and an expressed  
25 protein band of approximately 41 kDa was detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Clone "lv310\_7"

A polynucleotide of the present invention has been identified as clone "lv310\_7".  
30 Clones were first isolated from a human adult thyroid cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or were identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. Probes derived

from these cDNAs were then used to isolate lv310\_7 from a human adult brain cDNA library. lv310\_7 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "lv310\_7 protein").

The nucleotide sequence of lv310\_7 as presently determined is reported in SEQ ID NO:175, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the lv310\_7 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:176. Amino acids 269 to 281 of SEQ ID NO:176 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 282. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the lv310\_7 protein.

Another possible lv310\_7 reading frame and predicted amino acid sequence, encoded by base pairs 1619 to 2188 of SEQ ID NO:175, is reported in SEQ ID NO:283.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone lv310\_7 should be approximately 3650 bp.

The nucleotide sequence disclosed herein for lv310\_7 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. lv310\_7 demonstrated at least some similarity with sequences identified as N37001 (yy40a01.s1 Homo sapiens cDNA clone 273672 3'), R56228 (yg90d01.s1 Homo sapiens cDNA clone 40958 3'), and R56310 (yg90d01.r1 Homo sapiens cDNA clone 40958 5'). The predicted amino acid sequence disclosed herein for lv310\_7 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted lv310\_7 protein demonstrated at least some similarity to sequences identified as U24223 (alpha-CP1 [Homo sapiens]). Based upon sequence similarity, lv310\_7 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts 10 potential transmembrane domains within the lv310\_7 protein sequence, centered around amino acids 100, 130, 160, 210, 280, 490, 520, 600, 690, and 750 of SEQ ID NO:176, respectively.

Clone "nq34\_12"

A polynucleotide of the present invention has been identified as clone "nq34\_12". nq34\_12 was isolated from a human adult blood (erythroleukemia TF-1) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nq34\_12 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nq34\_12 protein").

The nucleotide sequence of nq34\_12 as presently determined is reported in SEQ ID NO:177, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nq34\_12 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:178. Amino acids 287 to 299 of SEQ ID NO:178 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 300. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nq34\_12 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nq34\_12 should be approximately 1700 bp.

The nucleotide sequence disclosed herein for nq34\_12 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nq34\_12 demonstrated at least some similarity with sequences identified as AA126375 (zl86c06.r1 Stratagene colon (#937204) Homo sapiens cDNA clone 511498 5'), AA446675 (zw84a08.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 783638 5'), AA448974 (zx07d05.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 785769 5' similar to SW YND0\_YEAST P40344 HYPOTHETICAL 35.9 KD PROTEIN IN RPC34-CSE2 INTERGENIC REGION), R57902 (F6699 Fetal heart Homo sapiens cDNA clone F6699 5' end), and X07453 (Plasmodium falciparum 11-1 gene part 1). The predicted amino acid sequence disclosed herein for nq34\_12 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted nq34\_12 protein demonstrated at least some similarity to sequences identified as X77395 (N2040 gene product [Saccharomyces cerevisiae]). Based

upon sequence similarity, nq34\_12 proteins and each similar protein or peptide may share at least some activity.

nq34\_12 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 34 kDa was detected in membrane fractions using SDS  
5 polyacrylamide gel electrophoresis.

Clone "pj154\_1"

A polynucleotide of the present invention has been identified as clone "pj154\_1". pj154\_1 was isolated from a human fetal carcinoma (NTD2 cells treated with retinoic acid  
10 for 23 days) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pj154\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pj154\_1 protein").

15 The nucleotide sequence of pj154\_1 as presently determined is reported in SEQ ID NO:179, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pj154\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:180. Amino acids 13 to 25 of SEQ ID NO:180 are a predicted leader/signal sequence, with the  
20 predicted mature amino acid sequence beginning at amino acid 26. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the pj154\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing  
25 clone pj154\_1 should be approximately 2300 bp.

The nucleotide sequence disclosed herein for pj154\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pj154\_1 demonstrated at least some similarity with sequences identified as AA223153 (zr07g12.r1 Stratagene NT2 neuronal precursor 937230 Homo  
30 sapiens cDNA clone 650854 5'), AA223170 (zr07g12.s1 Stratagene NT2 neuronal precursor 937230 Homo sapiens cDNA clone 650854 3' similar to contains Alu repetitive element), H16627 (ym26d04.r1 Homo sapiens cDNA clone 49469 5'), and Z44660 (H. sapiens partial cDNA sequence; clone c-26d11). Based upon sequence similarity, pj154\_1 proteins and



each similar protein or peptide may share at least some activity. The nucleotide sequence of pj154\_1 indicates that it may contain an Alu repetitive element.

Clone "pk147\_1"

5 A polynucleotide of the present invention has been identified as clone "pk147\_1". pk147\_1 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pk147\_1 is a  
10 full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pk147\_1 protein").

The nucleotide sequence of pk147\_1 as presently determined is reported in SEQ ID NO:181, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pk147\_1 protein  
15 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:182. Amino acids 16 to 28 of SEQ ID NO:182 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 29. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated  
20 from the remainder of the pk147\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pk147\_1 should be approximately 1600 bp.

The nucleotide sequence disclosed herein for pk147\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and  
25 FASTA search protocols. pk147\_1 demonstrated at least some similarity with sequences identified as AA126920 (zl23h01.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 502801 3'), AA406448 (zv12f07.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 753445 5'), and R51886 (yg78c03.s1 Homo sapiens cDNA clone 39574 3'). Based upon sequence similarity, pk147\_1 proteins and each similar protein or peptide may share at  
30 least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the pk147\_1 protein sequence centered around amino acid 37 of SEQ ID NO:182.

Clone "pt127\_1"

A polynucleotide of the present invention has been identified as clone "pt127\_1". pt127\_1 was isolated from a human adult blood (lymphoblastic leukemia MOLT-4) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pt127\_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pt127\_1 protein").

The nucleotide sequence of pt127\_1 as presently determined is reported in SEQ ID NO:183, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pt127\_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:184. Amino acids 8 to 20 of SEQ ID NO:184 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 21. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the pt127\_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pt127\_1 should be approximately 2600 bp.

The nucleotide sequence disclosed herein for pt127\_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pt127\_1 demonstrated at least some similarity with sequences identified as AA081843 (zn19g10.r1 Stratagene neuroepithelium NT2RAMI 937234 Homo sapiens cDNA clone 547938 5') and R39258 (yc91h08.s1 Homo sapiens cDNA clone 23514 3'). Based upon sequence similarity, pt127\_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts five additional potential transmembrane domains within the pt127\_1 protein sequence centered around amino acids 60, 100, 130, 190, and 240 of SEQ ID NO:184.

Clone "qo115\_13"

A polynucleotide of the present invention has been identified as clone "qo115\_13". qo115\_13 was isolated from a human adult brain (corpus callosum) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No.

5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. qo115\_13 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "qo115\_13 protein").

5        The nucleotide sequence of qo115\_13 as presently determined is reported in SEQ ID NO:185, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the qo115\_13 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:186. Amino acids 29 to 41 of SEQ ID NO:186 are a predicted leader/signal sequence, with the  
10 predicted mature amino acid sequence beginning at amino acid 42. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the qo115\_13 protein.

      The EcoRI/NotI restriction fragment obtainable from the deposit containing  
15 clone qo115\_13 should be approximately 1200 bp.

      The nucleotide sequence disclosed herein for qo115\_13 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. No significant hits were found in the database. The nucleotide sequence of qo115\_13 indicates that it may contain repetitive elements.  
20

#### Deposit of Clones

      Clones bd306\_7, fj283\_11, fk317\_3, k213\_2x, na316\_1, nf93\_20, np164\_1, pe204\_1, ya1\_1, and yb8\_1 were deposited on November 26, 1997 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.)  
25 as an original deposit under the Budapest Treaty and were given the accession number 98599, from which each clone comprising a particular polynucleotide is obtainable. Clone fj283\_6 was deposited on 17 November, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and was given the accession number 98988.  
30        Clones am856\_3, am996\_12, cc69\_1, cc162\_1, if87\_1, nn103\_4, np206\_8, nt746\_4, pe286\_1, and yb7\_1 were deposited on December 4, 1997 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.)

as an original deposit under the Budapest Treaty and were given the accession number 98600, from which each clone comprising a particular polynucleotide is obtainable.

Clones am728\_60, bf377\_1, cw354\_1, nm134\_4, yb11\_1, and yc2\_1 were deposited on December 19, 1997 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98621, from which each clone comprising a particular polynucleotide is obtainable.

Clones ff168\_12, ls9\_1, na1010\_1, nf87\_1, nh796\_1, nn229\_1, and np156\_1 were deposited on December 31, 1997 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98623, from which each clone comprising a particular polynucleotide is obtainable.

Clones bg570\_1, bi120\_2, bn594\_1, en554\_1, na474\_10, nn16\_10, np189\_9, ny226\_1, pe159\_1, and pj314\_8 were deposited on January 7, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98629, from which each clone comprising a particular polynucleotide is obtainable.

Clones bp870\_2, bx141\_2, cw272\_7, rh328\_5, nm214\_3, nn320\_2, pp392\_3, ya13\_1, yb37\_1, and yb39\_1 were deposited on January 8, 1998 with the American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98630, from which each clone comprising a particular polynucleotide is obtainable. Clone bp870\_1 was deposited on April 7, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and was given the accession number 98724, from which deposit the bp870\_1 clone comprising a particular polynucleotide is obtainable.

Clones bd577\_1, bv280\_3, co315\_3, ij226\_6, nf443\_1, nt429\_1, pe503\_1, pe834\_6, ya10\_1, and yb40\_1 were deposited on January 13, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98631, from which each clone comprising a particular polynucleotide is obtainable.

Clones cs756\_2, ew150\_1, gg894\_13, it217\_2, ml235\_2, mt24\_2, pe584\_2, pj323\_2, yb24\_1, and yb44\_1 were deposited on January 22, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 5 98636, from which each clone comprising a particular polynucleotide is obtainable.

Clones bn69\_15, cb110\_1, ch4\_11, cn621\_8, gy621\_1, hb1041\_2, mh703\_1, na461\_19, na492\_2, and na669\_10 were deposited on January 30, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the 10 accession number 98647, from which each clone comprising a particular polynucleotide is obtainable.

Clones co821\_31, dk329\_1, fx317\_11, lp547\_4, lv310\_7, nq34\_12, pj154\_1, pk147\_1, pt127\_1, and qo115\_13 were deposited on February 18, 1998 with the American Type Culture Collection (10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) 15 as an original deposit under the Budapest Treaty and were given the accession number ATCC 98663, from which each clone comprising a particular polynucleotide is obtainable.

All restrictions on the availability to the public of the deposited material will be irrevocably removed upon the granting of the patent, except for the requirements specified in 37 C.F.R. § 1.808(b), and the term of the deposit will comply with 37 C.F.R. § 20 1.806.

Each clone has been transfected into separate bacterial cells (*E. coli*) in these composite deposits. Each clone can be removed from the vector in which it was deposited by performing an EcoRI/NotI digestion (5' site, EcoRI; 3' site, NotI) to produce the appropriate fragment for such clone. Each clone was deposited in either the pED6 or 25 pNOTs vector depicted in Figures 1A and 1B, respectively. The pED6dpc2 vector ("pED6") was derived from pED6dpc1 by insertion of a new polylinker to facilitate cDNA cloning (Kaufman *et al.*, 1991, *Nucleic Acids Res.* 19: 4485-4490); the pNOTs vector was derived from pMT2 (Kaufman *et al.*, 1989, *Mol. Cell. Biol.* 9: 946-958) by deletion of the DHFR sequences, insertion of a new polylinker, and insertion of the M13 origin of 30 replication in the ClaI site. In some instances, the deposited clone can become "flipped" (i.e., in the reverse orientation) in the deposited isolate. In such instances, the cDNA insert can still be isolated by digestion with EcoRI and NotI. However, NotI will then produce the 5' site and EcoRI will produce the 3' site for placement of the cDNA in proper

orientation for expression in a suitable vector. The cDNA may also be expressed from the vectors in which they were deposited.

Bacterial cells containing a particular clone can be obtained from the composite deposit as follows:

- 5 An oligonucleotide probe or probes should be designed to the sequence that is known for that particular clone. This sequence can be derived from the sequences provided herein, or from a combination of those sequences. The sequence of an oligonucleotide probe that was used to isolate or to sequence each full-length clone is identified below, and should be most reliable in isolating the clone of interest.

10	<u>Clone</u>	<u>Probe Sequence</u>
	bd306_7	SEQ ID NO:187
	fj283_11	SEQ ID NO:188
	fj283_6	SEQ ID NO:197
15	fk317_3	SEQ ID NO:189
	k213_2x	SEQ ID NO:190
	na316_1	SEQ ID NO:191
	nf93_20	SEQ ID NO:192
	np164_1	SEQ ID NO:193
20	pe204_1	SEQ ID NO:194
	ya1_1	SEQ ID NO:195
	yb8_1	SEQ ID NO:196
	am856_3	SEQ ID NO:199
	am996_12	SEQ ID NO:200
25	cc69_1	SEQ ID NO:201
	cc162_1	SEQ ID NO:202
	if87_1	SEQ ID NO:203
	nn103_4	SEQ ID NO:204
	np206_8	SEQ ID NO:205
30	nt746_4	SEQ ID NO:206
	pe286_1	SEQ ID NO:207
	yb7_1	SEQ ID NO:208
	am728_60	SEQ ID NO:209

	cw354_1	SEQ ID NO:210
	nm134_4	SEQ ID NO:211
	yb11_1	SEQ ID NO:212
	yc2_1	SEQ ID NO:213
5	ff168_12	SEQ ID NO:214
	ls9_1	SEQ ID NO:215
	na1010_1	SEQ ID NO:216
	nf87_1	SEQ ID NO:217
	nh796_1	SEQ ID NO:218
10	nn229_1	SEQ ID NO:219
	np156_1	SEQ ID NO:220
	bi120_2	SEQ ID NO:221
	na474_10	SEQ ID NO:222
	nn16_10	SEQ ID NO:223
15	np189_9	SEQ ID NO:224
	ny226_1	SEQ ID NO:225
	pe159_1	SEQ ID NO:226
	pj314_8	SEQ ID NO:227
	bp870_1	SEQ ID NO:228
20	bx141_2	SEQ ID NO:229
	cw272_7	SEQ ID NO:230
	nh328_5	SEQ ID NO:231
	nm214_3	SEQ ID NO:232
	nn320_2	SEQ ID NO:233
25	pp392_3	SEQ ID NO:234
	yb37_1	SEQ ID NO:235
	bd577_1	SEQ ID NO:236
	bv280_3	SEQ ID NO:237
	co315_3	SEQ ID NO:238
30	ij226_6	SEQ ID NO:239
	nf443_1	SEQ ID NO:240
	nt429_1	SEQ ID NO:241
	pe503_1	SEQ ID NO:242

	pe834_6	SEQ ID NO:243
	yb40_1	SEQ ID NO:244
	cs756_2	SEQ ID NO:245
	ew150_1	SEQ ID NO:246
5	gg894_13	SEQ ID NO:247
	it217_2	SEQ ID NO:248
	ml235_2	SEQ ID NO:249
	mt24_2	SEQ ID NO:250
	pe584_2	SEQ ID NO:251
10	pj323_2	SEQ ID NO:252
	yb24_1	SEQ ID NO:253
	bn69_15	SEQ ID NO:254
	cb110_1	SEQ ID NO:255
	ch4_11	SEQ ID NO:256
15	cn621_8	SEQ ID NO:257
	gy621_1	SEQ ID NO:258
	hb1041_2	SEQ ID NO:259
	mh703_1	SEQ ID NO:260
	na461_19	SEQ ID NO:261
20	na492_2	SEQ ID NO:262
	na669_10	SEQ ID NO:263
	co821_31	SEQ ID NO:264
	dk329_1	SEQ ID NO:265
	fx317_11	SEQ ID NO:266
25	lp547_4	SEQ ID NO:267
	lv310_7	SEQ ID NO:268
	nq34_12	SEQ ID NO:269
	pj154_1	SEQ ID NO:270
	pk147_1	SEQ ID NO:271
30	pt127_1	SEQ ID NO:272
	qol15_13	SEQ ID NO:273



In the sequences listed above which include an N at position 2, that position is occupied in preferred probes/primers by a biotinylated phosphoramidite residue rather than a nucleotide (such as, for example, that produced by use of biotin phosphoramidite (1-dimethoxytrityloxy-2-(N-biotinyl-4-aminobutyl)-propyl-3-O-(2-cyanoethyl)-(N,N-diisopropyl)-phosphoramidite) (Glen Research, cat. no. 10-1953)).

The design of the oligonucleotide probe should preferably follow these parameters:

- (a) It should be designed to an area of the sequence which has the fewest ambiguous bases ("N's"), if any;
- (b) It should be designed to have a  $T_m$  of approx. 80 ° C (assuming 2° for each A or T and 4 degrees for each G or C).

The oligonucleotide should preferably be labeled with  $\gamma$ - $^{32}\text{P}$  ATP (specific activity 6000 Ci/mmol) and T4 polynucleotide kinase using commonly employed techniques for labeling oligonucleotides. Other labeling techniques can also be used. Unincorporated label should preferably be removed by gel filtration chromatography or other established methods. The amount of radioactivity incorporated into the probe should be quantitated by measurement in a scintillation counter. Preferably, specific activity of the resulting probe should be approximately  $4\text{e}+6$  dpm/pmol.

The bacterial culture containing the pool of full-length clones should preferably be thawed and 100  $\mu\text{l}$  of the stock used to inoculate a sterile culture flask containing 25 ml of sterile L-broth containing ampicillin at 100  $\mu\text{g}/\text{ml}$ . The culture should preferably be grown to saturation at 37°C, and the saturated culture should preferably be diluted in fresh L-broth. Aliquots of these dilutions should preferably be plated to determine the dilution and volume which will yield approximately 5000 distinct and well-separated colonies on solid bacteriological media containing L-broth containing ampicillin at 100  $\mu\text{g}/\text{ml}$  and agar at 1.5% in a 150 mm petri dish when grown overnight at 37°C. Other known methods of obtaining distinct, well-separated colonies can also be employed.

Standard colony hybridization procedures should then be used to transfer the colonies to nitrocellulose filters and lyse, denature and bake them.

The filter is then preferably incubated at 65°C for 1 hour with gentle agitation in 6X SSC (20X stock is 175.3 g NaCl/liter, 88.2 g Na citrate/liter, adjusted to pH 7.0 with NaOH) containing 0.5% SDS, 100  $\mu\text{g}/\text{ml}$  of yeast RNA, and 10 mM EDTA (approximately 10 mL per 150 mm filter). Preferably, the probe is then added to the hybridization mix

at a concentration greater than or equal to  $1e+6$  dpm/mL. The filter is then preferably incubated at  $65^{\circ}\text{C}$  with gentle agitation overnight. The filter is then preferably washed in 500 mL of 2X SSC/0.5% SDS at room temperature without agitation, preferably followed by 500 mL of 2X SSC/0.1% SDS at room temperature with gentle shaking for 15  
5 minutes. A third wash with 0.1X SSC/0.5% SDS at  $65^{\circ}\text{C}$  for 30 minutes to 1 hour is optional. The filter is then preferably dried and subjected to autoradiography for sufficient time to visualize the positives on the X-ray film. Other known hybridization methods can also be employed.

The positive colonies are picked, grown in culture, and plasmid DNA isolated  
10 using standard procedures. The clones can then be verified by restriction analysis, hybridization analysis, or DNA sequencing.

Fragments of the proteins of the present invention which are capable of exhibiting biological activity are also encompassed by the present invention. Fragments of the protein may be in linear form or they may be cyclized using known methods, for example,  
15 as described in H.U. Saragovi, *et al.*, Bio/Technology 10, 773-778 (1992) and in R.S. McDowell, *et al.*, J. Amer. Chem. Soc. 114, 9245-9253 (1992), both of which are incorporated herein by reference. Such fragments may be fused to carrier molecules such as immunoglobulins for many purposes, including increasing the valency of protein binding sites. For example, fragments of the protein may be fused through "linker"  
20 sequences to the Fc portion of an immunoglobulin. For a bivalent form of the protein, such a fusion could be to the Fc portion of an IgG molecule. Other immunoglobulin isotypes may also be used to generate such fusions. For example, a protein - IgM fusion would generate a decavalent form of the protein of the invention.

The present invention also provides both full-length and mature forms of the  
25 disclosed proteins. The full-length form of the such proteins is identified in the sequence listing by translation of the nucleotide sequence of each disclosed clone. The mature form(s) of such protein may be obtained by expression of the disclosed full-length polynucleotide (preferably those deposited with ATCC) in a suitable mammalian cell or other host cell. The sequence(s) of the mature form(s) of the protein may also be  
30 determinable from the amino acid sequence of the full-length form.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are

derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can  
5 be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or primers from the disclosed sequence information for identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of  
10 the organism from which the gene was isolated.

The chromosomal location corresponding to the polynucleotide sequences disclosed herein may also be determined, for example by hybridizing appropriately labeled polynucleotides of the present invention to chromosomes *in situ*. It may also be possible to determine the corresponding chromosomal location for a disclosed  
15 polynucleotide by identifying significantly similar nucleotide sequences in public databases, such as expressed sequence tags (ESTs), that have already been mapped to particular chromosomal locations. For at least some of the polynucleotide sequences disclosed herein, public database sequences having at least some similarity to the polynucleotide of the present invention have been listed by database accession number.  
20 Searches using the GenBank accession numbers of these public database sequences can then be performed at an Internet site provided by the National Center for Biotechnology Information having the address <http://www.ncbi.nlm.nih.gov/UniGene/>, in order to identify "UniGene clusters" of overlapping sequences. Many of the "UniGene clusters" so identified will already have been mapped to particular chromosomal sites.

25 Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Morris, 1994, *Trends Pharmacol. Sci.* 15(7): 250-254; Lavarosky *et al.*, 1997,  
30 *Biochem. Mol. Med.* 62(1): 11-22; and Hampel, 1998, *Prog. Nucleic Acid Res. Mol. Biol.* 58: 1-39; all of which are incorporated by reference herein). Transgenic animals that have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are

stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein).

5 In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished through insertion, preferably followed by imprecise excision, of

10 transposable elements (Plasterk, 1992, *Bioessays* 14(9): 629-633; Zwaal *et al.*, 1993, *Proc. Natl. Acad. Sci. USA* 90(16): 7431-7435; Clark *et al.*, 1994, *Proc. Natl. Acad. Sci. USA* 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour *et al.*, 1988, *Nature* 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059;

15 5,631,153; 5,614,396; 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identification of molecules that interact with the

20 protein product(s) of the corresponding gene(s).

Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms, part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and

25 transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information. For example, the TopPredII computer program can be used to predict the location of transmembrane domains in an amino acid sequence, domains which are described by the location of the center of the transmembrane domain, with at least ten transmembrane

30 amino acids on each side of the reported central residue(s).

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of a disclosed protein and have at least 60%

sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

10 In particular, sequence identity may be determined using WU-BLAST (Washington University BLAST) version 2.0 software, which builds upon WU-BLAST version 1.4, which in turn is based on the public domain NCBI-BLAST version 1.4 (Altschul and Gish, 1996, Local alignment statistics, Doolittle *ed.*, *Methods in Enzymology* 266: 460-480; Altschul *et al.*, 1990, Basic local alignment search tool, *Journal of*  
15 *Molecular Biology* 215: 403-410; Gish and States, 1993, Identification of protein coding regions by database similarity search, *Nature Genetics* 3: 266-272; Karlin and Altschul, 1993, Applications and statistics for multiple high-scoring segments in molecular sequences, *Proc. Natl. Acad. Sci. USA* 90: 5873-5877; all of which are incorporated by reference herein). WU-BLAST version 2.0 executable programs for several UNIX  
20 platforms can be downloaded from <ftp://blast.wustl.edu/blast/executables>. The complete suite of search programs (BLASTP, BLASTN, BLASTX, TBLASTN, and TBLASTX) is provided at that site, in addition to several support programs. WU-BLAST 2.0 is copyrighted and may not be sold or redistributed in any form or manner without the express written consent of the author; but the posted executables may otherwise be freely used for  
25 commercial, nonprofit, or academic purposes. In all search programs in the suite -- BLASTP, BLASTN, BLASTX, TBLASTN and TBLASTX -- the gapped alignment routines are integral to the database search itself, and thus yield much better sensitivity and selectivity while producing the more easily interpreted output. Gapping can optionally be turned off in all of these programs, if desired. The default penalty (Q) for a gap of length  
30 one is Q=9 for proteins and BLASTP, and Q=10 for BLASTN, but may be changed to any integer value including zero, one through eight, nine, ten, eleven, twelve through twenty, twenty-one through fifty, fifty-one through one hundred, etc. The default per-residue

penalty for extending a gap (R) is  $R=2$  for proteins and BLASTP, and  $R=10$  for BLASTN, but may be changed to any integer value including zero, one, two, three, four, five, six, seven, eight, nine, ten, eleven, twelve through twenty, twenty-one through fifty, fifty-one through one hundred, etc. Any combination of values for Q and R can be used in order  
5 to align sequences so as to maximize overlap and identity while minimizing sequence gaps. The default amino acid comparison matrix is BLOSUM62, but other amino acid comparison matrices such as PAM can be utilized.

Species homologues of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or  
10 polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide. Preferably, polynucleotide species homologues have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% identity) with the given polynucleotide, and protein species homologues have at least 30% sequence  
15 identity (more preferably, at least 45% identity; most preferably at least 60% identity) with the given protein, where sequence identity is determined by comparing the nucleotide sequences of the polynucleotides or the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Species homologues may be isolated and identified by making suitable probes or primers from the  
20 sequences provided herein and screening a suitable nucleic acid source from the desired species. Preferably, species homologues are those isolated from mammalian species. Most preferably, species homologues are those isolated from certain mammalian species such as, for example, *Pan troglodytes*, *Gorilla gorilla*, *Pongo pygmaeus*, *Hylobates concolor*, *Macaca mulatta*, *Papio papio*, *Papio hamadryas*, *Cercopithecus aethiops*, *Cebus capucinus*, *Aotus*  
25 *trivirgatus*, *Sanguinus oedipus*, *Microcebus murinus*, *Mus musculus*, *Rattus norvegicus*, *Cricetulus griseus*, *Felis catus*, *Mustela vison*, *Canis familiaris*, *Oryctolagus cuniculus*, *Bos taurus*, *Ovis aries*, *Sus scrofa*, and *Equus caballus*, for which genetic maps have been created allowing the identification of syntenic relationships between the genomic organization of genes in one species and the genomic organization of the related genes in another species  
30 (O'Brien and Seuánez, 1988, *Ann. Rev. Genet.* 22: 323-351; O'Brien *et al.*, 1993, *Nature Genetics* 3:103-112; Johansson *et al.*, 1995, *Genomics* 25: 682-690; Lyons *et al.*, 1997, *Nature Genetics* 15: 47-56; O'Brien *et al.*, 1997, *Trends in Genetics* 13(10): 393-399; Carver and Stubbs, 1997, *Genome Research* 7:1123-1137; all of which are incorporated by reference herein).

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotides which also encode proteins which are identical or have significantly similar sequences to those encoded by the disclosed polynucleotides. Preferably, allelic variants have at least  
5 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% identity) with the given polynucleotide, where sequence identity is determined by comparing the nucleotide sequences of the polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps. Allelic variants may be isolated and identified by making suitable probes or primers from the sequences  
10 provided herein and screening a suitable nucleic acid source from individuals of the appropriate species.

The invention also includes polynucleotides with sequences complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides that hybridize under reduced  
15 stringency conditions, more preferably stringent conditions, and most preferably highly stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the table below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least  
20 as stringent as, for example, conditions M-R.

Stringency Condition	Polynucleotide Hybrid	Hybrid Length (bp) <sup>†</sup>	Hybridization Temperature and Buffer <sup>†</sup>	Wash Temperature and Buffer <sup>†</sup>
5	A	≥ 50	65°C; 1xSSC -or- 42°C; 1xSSC, 50% formamide	65°C; 0.3xSSC
	B	<50	T <sub>B</sub> <sup>*</sup> ; 1xSSC	T <sub>B</sub> <sup>*</sup> ; 1xSSC
	C	≥ 50	67°C; 1xSSC -or- 45°C; 1xSSC, 50% formamide	67°C; 0.3xSSC
	D	<50	T <sub>D</sub> <sup>*</sup> ; 1xSSC	T <sub>D</sub> <sup>*</sup> ; 1xSSC
	E	≥ 50	70°C; 1xSSC -or- 50°C; 1xSSC, 50% formamide	70°C; 0.3xSSC
	F	<50	T <sub>F</sub> <sup>*</sup> ; 1xSSC	T <sub>F</sub> <sup>*</sup> ; 1xSSC
10	G	≥ 50	65°C; 4xSSC -or- 42°C; 4xSSC, 50% formamide	65°C; 1xSSC
	H	<50	T <sub>H</sub> <sup>*</sup> ; 4xSSC	T <sub>H</sub> <sup>*</sup> ; 4xSSC
	I	≥ 50	67°C; 4xSSC -or- 45°C; 4xSSC, 50% formamide	67°C; 1xSSC
	J	<50	T <sub>J</sub> <sup>*</sup> ; 4xSSC	T <sub>J</sub> <sup>*</sup> ; 4xSSC
	K	≥ 50	70°C; 4xSSC -or- 50°C; 4xSSC, 50% formamide	67°C; 1xSSC
	L	<50	T <sub>L</sub> <sup>*</sup> ; 2xSSC	T <sub>L</sub> <sup>*</sup> ; 2xSSC
15	M	≥ 50	50°C; 4xSSC -or- 40°C; 6xSSC, 50% formamide	50°C; 2xSSC
	N	<50	T <sub>N</sub> <sup>*</sup> ; 6xSSC	T <sub>N</sub> <sup>*</sup> ; 6xSSC
	O	≥ 50	55°C; 4xSSC -or- 42°C; 6xSSC, 50% formamide	55°C; 2xSSC
	P	<50	T <sub>P</sub> <sup>*</sup> ; 6xSSC	T <sub>P</sub> <sup>*</sup> ; 6xSSC
	Q	≥ 50	60°C; 4xSSC -or- 45°C; 6xSSC, 50% formamide	60°C; 2xSSC
	R	<50	T <sub>R</sub> <sup>*</sup> ; 4xSSC	T <sub>R</sub> <sup>*</sup> ; 4xSSC

<sup>†</sup>: The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.

<sup>†</sup>: SSPE (1xSSPE is 0.15M NaCl, 10mM NaH<sub>2</sub>PO<sub>4</sub>, and 1.25mM EDTA, pH 7.4) can be substituted for SSC (1xSSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.

<sup>\*</sup>T<sub>B</sub> - T<sub>R</sub>: The hybridization temperature for hybrids anticipated to be less than 50 base pairs in length should be 5-10°C less than the melting temperature (T<sub>m</sub>) of the hybrid, where T<sub>m</sub> is determined according to the following equations. For hybrids less than 18 base pairs in length, T<sub>m</sub>(°C) = 2(# of A + T bases) + 4(# of G + C bases). For hybrids between 18 and 49 base pairs in length, T<sub>m</sub>(°C) = 81.5 + 16.6(log<sub>10</sub>[Na<sup>+</sup>]) + 0.41(%G+C) - (600/N), where N is the number of bases in the hybrid, and [Na<sup>+</sup>] is the concentration of sodium ions in the hybridization buffer ([Na<sup>+</sup>] for 1xSSC = 0.165 M).



Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and *Current Protocols in Molecular Biology*, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

The isolated polynucleotide of the invention may be operably linked to an expression control sequence such as the pMT2 or pED expression vectors disclosed in Kaufman *et al.*, *Nucleic Acids Res.* 19, 4485-4490 (1991), in order to produce the protein recombinantly. Many suitable expression control sequences are known in the art. General methods of expressing recombinant proteins are also known and are exemplified in R. Kaufman, *Methods in Enzymology* 185, 537-566 (1990). As defined herein "operably linked" means that the isolated polynucleotide of the invention and an expression control sequence are situated within a vector or cell in such a way that the protein is expressed by a host cell which has been transformed (transfected) with the ligated polynucleotide/expression control sequence.

A number of types of cells may act as suitable host cells for expression of the protein. Mammalian host cells include, for example, monkey COS cells, Chinese Hamster Ovary (CHO) cells, human kidney 293 cells, human epidermal A431 cells, human Colo205 cells, 3T3 cells, CV-1 cells, other transformed primate cell lines, normal diploid cells, cell strains derived from *in vitro* culture of primary tissue, primary explants, HeLa cells, mouse L cells, BHK, HL-60, U937, HaK or Jurkat cells.

Alternatively, it may be possible to produce the protein in lower eukaryotes such as yeast or in prokaryotes such as bacteria. Potentially suitable yeast strains include *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Kluyveromyces* strains, *Candida*, or any yeast strain capable of expressing heterologous proteins. Potentially suitable bacterial

strains include *Escherichia coli*, *Bacillus subtilis*, *Salmonella typhimurium*, or any bacterial strain capable of expressing heterologous proteins. If the protein is made in yeast or bacteria, it may be necessary to modify the protein produced therein, for example by phosphorylation or glycosylation of the appropriate sites, in order to obtain the functional protein. Such covalent attachments may be accomplished using known chemical or enzymatic methods.

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, e.g., Invitrogen, San Diego, California, U.S.A. (the MaxBac® kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucleotide of the present invention is "transformed."

The protein of the invention may be prepared by culturing transformed host cells under culture conditions suitable to express the recombinant protein. The resulting expressed protein may then be purified from such culture (i.e., from culture medium or cell extracts) using known purification processes, such as gel filtration and ion exchange chromatography. The purification of the protein may also include an affinity column containing agents which will bind to the protein; one or more column steps over such affinity resins as concanavalin A-agarose, heparin-toyopearl® or Cibacrom blue 3GA Sepharose®; one or more steps involving hydrophobic interaction chromatography using such resins as phenyl ether, butyl ether, or propyl ether; or immunoaffinity chromatography.

Alternatively, the protein of the invention may also be expressed in a form which will facilitate purification. For example, it may be expressed as a fusion protein, such as those of maltose binding protein (MBP), glutathione-S-transferase (GST) or thioredoxin (TRX). Kits for expression and purification of such fusion proteins are commercially available from New England BioLabs (Beverly, MA), Pharmacia (Piscataway, NJ) and Invitrogen Corporation (Carlsbad, CA), respectively. The protein can also be tagged with an epitope and subsequently purified by using a specific antibody directed to such epitope. One such epitope ("Flag") is commercially available from the Eastman Kodak Company (New Haven, CT).

Finally, one or more reverse-phase high performance liquid chromatography (RP-HPLC) steps employing hydrophobic RP-HPLC media, e.g., silica gel having pendant methyl or other aliphatic groups, can be employed to further purify the protein. Some or all of the foregoing purification steps, in various combinations, can also be employed to provide a substantially homogeneous isolated recombinant protein. The protein thus purified is substantially free of other mammalian proteins and is defined in accordance with the present invention as an "isolated protein."

The protein of the invention may also be expressed as a product of transgenic animals, e.g., as a component of the milk of transgenic cows, goats, pigs, or sheep which are characterized by somatic or germ cells containing a nucleotide sequence encoding the protein.

The protein may also be produced by known conventional chemical synthesis. Methods for constructing the proteins of the present invention by synthetic means are known to those skilled in the art. The synthetically-constructed protein sequences, by virtue of sharing primary, secondary or tertiary structural and/or conformational characteristics with proteins may possess biological properties in common therewith, including protein activity. Thus, they may be employed as biologically active or immunological substitutes for natural, purified proteins in screening of therapeutic compounds and in immunological processes for the development of antibodies.

The proteins provided herein also include proteins characterized by amino acid sequences similar to those of purified proteins but into which modification are naturally provided or deliberately engineered. For example, modifications in the peptide or DNA sequences can be made by those skilled in the art using known techniques. Modifications of interest in the protein sequences may include the alteration, substitution, replacement, insertion or deletion of a selected amino acid residue in the coding sequence. For example, one or more of the cysteine residues may be deleted or replaced with another amino acid to alter the conformation of the molecule. Techniques for such alteration, substitution, replacement, insertion or deletion are well known to those skilled in the art (see, e.g., U.S. Patent No. 4,518,584). Preferably, such alteration, substitution, replacement, insertion or deletion retains the desired activity of the protein.

Other fragments and derivatives of the sequences of proteins which would be expected to retain protein activity in whole or in part and may thus be useful for screening or other immunological methodologies may also be easily made by those skilled in the art.

given the disclosures herein. Such modifications are believed to be encompassed by the present invention.

### USES AND BIOLOGICAL ACTIVITY

5       The polynucleotides and proteins of the present invention are expected to exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors  
10   suitable for introduction of DNA).

#### Research Uses and Utilities

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant  
15   protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA  
20   sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression  
25   patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, those described in Gyuris *et al.*, 1993, *Cell* 75:  
30   791-803 and in Rossi *et al.*, 1997, *Proc. Natl. Acad. Sci. USA* 94: 8405-8410, all of which are incorporated by reference herein) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

#### Nutritional Uses

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

#### Cytokine and Cell Proliferation/Differentiation Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may

induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor-dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK. The activity of a protein of the invention may, among other means, be measured by the following methods:

- 10        Assays for T-cell or thymocyte proliferation include without limitation those described in: *Current Protocols in Immunology*, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., *J. Immunol.* 137:3494-3500, 1986;
- 15    Bertagnolli et al., *J. Immunol.* 145:1706-1712, 1990; Bertagnolli et al., *Cellular Immunology* 133:327-341, 1991; Bertagnolli, et al., *J. Immunol.* 149:3778-3783, 1992; Bowman et al., *J. Immunol.* 152: 1756-1761, 1994.

- Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon  $\gamma$ , Schreiber, R.D. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

- Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., *J. Exp. Med.* 173:1205-1211, 1991; Moreau et al., *Nature* 336:690-692, 1988; Greenberger et al., *Proc. Natl. Acad. Sci. U.S.A.* 80:2931-2938, 1983;
- 25    Measurement of mouse and human interleukin 6 - Nordan, R. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991;
  - 30    Smith et al., *Proc. Natl. Acad. Sci. U.S.A.* 83:1857-1861, 1986; Measurement of human Interleukin 11 - Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In *Current Protocols*

in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

- 5        Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: *Current Protocols in Immunology*, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience
- 10    (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

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#### Immune Stimulating or Suppressing Activity

- A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral,
- 20    bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, *Leishmania* spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.
- 25    Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitus,
- 30

myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for  
5 example, organ transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be possible to regulate immune responses in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction  
10 of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is  
15 distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without  
20 limitation B lymphocyte antigen functions (such as, for example, B7)), *e.g.*, preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated  
25 through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (*e.g.*, B7-  
30 1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an



immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or  
5 tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in  
10 rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins *in vivo* as described in Lenschow *et al.*, Science 257:789-792 (1992) and Turka *et al.*, Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the  
15 effect of blocking B lymphocyte antigen function *in vivo* on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production  
20 of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor:ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which  
25 may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune  
30 encephalitis, systemic lupus erythematosus in MRL/*lpr/lpr* mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells *in vitro* with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the *in vitro* activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells *in vivo*.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (*e.g.*, sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected *ex vivo* with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection *in vivo*.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the

transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I  $\alpha$  chain protein and  $\beta_2$  microglobulin protein or an MHC class II  $\alpha$  chain protein and an MHC class II  $\beta$  chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowman et al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: *In vitro*

antibody production, Mond, J.J. and Brunswick, M. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: *Current Protocols in Immunology*, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., *J. Immunol.* 137:3494-3500, 1986; Takai et al., *J. Immunol.* 140:508-512, 1988; Bertagnolli et al., *J. Immunol.* 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., *J. Immunol.* 134:536-544, 1995; Inaba et al., *Journal of Experimental Medicine* 173:549-559, 1991; Macatonia et al., *Journal of Immunology* 154:5071-5079, 1995; Porgador et al., *Journal of Experimental Medicine* 182:255-260, 1995; Nair et al., *Journal of Virology* 67:4062-4069, 1993; Huang et al., *Science* 264:961-965, 1994; Macatonia et al., *Journal of Experimental Medicine* 169:1255-1264, 1989; Bhardwaj et al., *Journal of Clinical Investigation* 94:797-807, 1994; and Inaba et al., *Journal of Experimental Medicine* 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., *Cytometry* 13:795-808, 1992; Gorczyca et al., *Leukemia* 7:659-670, 1993; Gorczyca et al., *Cancer Research* 53:1945-1951, 1993; Itoh et al., *Cell* 66:233-243, 1991; Zacharchuk, *Journal of Immunology* 145:4037-4045, 1990; Zamai et al., *Cytometry* 14:891-897, 1993; Gorczyca et al., *International Journal of Oncology* 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., *Blood* 84:111-117, 1994; Fine et al., *Cellular Immunology* 155:111-122, 1994; Galy et al., *Blood* 85:2770-2778, 1995; Toki et al., *Proc. Nat. Acad. Sci. USA* 88:7548-7551, 1991.

### Hematopoiesis Regulating Activity

A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even

marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either *in-vivo* or *ex-vivo* (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M.G. In *Culture of Hematopoietic Cells*. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama

- et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In *Culture of Hematopoietic Cells*. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R.E. In *Culture of Hematopoietic Cells*. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In *Culture of Hematopoietic Cells*. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In *Culture of Hematopoietic Cells*. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

#### Tissue Growth Activity

A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. *De novo* bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors *ex vivo* for return *in vivo* to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, *i.e.* for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein of the present invention may also exhibit activity for  
5 generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also  
10 exhibit angiogenic activity.

A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein of the present invention may also be useful for promoting or inhibiting  
15 differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for tissue generation activity include, without limitation, those described  
20 in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon); International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in:  
Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year  
25 Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

#### Activin/Inhibin Activity

A protein of the present invention may also exhibit activin- or inhibin-related  
30 activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin  $\alpha$  family, may be useful



as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- $\beta$  group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

10 The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., *Endocrinology* 91:562-572, 1972; Ling et al., *Nature* 321:779-782, 1986; Vale et al., *Nature* 321:776-779, 1986; Mason et al., *Nature* 318:659-663, 1985; Forage et al., *Proc. Natl. Acad. Sci. USA* 83:3091-3095, 1986.

#### Chemotactic/Chemokinetic Activity

A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al. Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

#### Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

#### Receptor/Ligand Activity

A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their

ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

10 The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and  
15 Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

#### 20 Anti-Inflammatory Activity

Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the  
25 inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic  
30 inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over

production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

#### Cadherin/Tumor Invasion Suppressor Activity

5 Cadherins are calcium-dependent adhesion molecules that appear to play major roles during development, particularly in defining specific cell types. Loss or alteration of normal cadherin expression can lead to changes in cell adhesion properties linked to tumor growth and metastasis. Cadherin malfunction is also implicated in other human diseases, such as pemphigus vulgaris and pemphigus foliaceus (auto-immune blistering  
10 skin diseases), Crohn's disease, and some developmental abnormalities.

The cadherin superfamily includes well over forty members, each with a distinct pattern of expression. All members of the superfamily have in common conserved extracellular repeats (cadherin domains), but structural differences are found in other parts of the molecule. The cadherin domains bind calcium to form their tertiary structure and  
15 thus calcium is required to mediate their adhesion. Only a few amino acids in the first cadherin domain provide the basis for homophilic adhesion; modification of this recognition site can change the specificity of a cadherin so that instead of recognizing only itself, the mutant molecule can now also bind to a different cadherin. In addition, some cadherins engage in heterophilic adhesion with other cadherins.

20 E-cadherin, one member of the cadherin superfamily, is expressed in epithelial cell types. Pathologically, if E-cadherin expression is lost in a tumor, the malignant cells become invasive and the cancer metastasizes. Transfection of cancer cell lines with polynucleotides expressing E-cadherin has reversed cancer-associated changes by returning altered cell shapes to normal, restoring cells' adhesiveness to each other and to  
25 their substrate, decreasing the cell growth rate, and drastically reducing anchorage-independent cell growth. Thus, reintroducing E-cadherin expression reverts carcinomas to a less advanced stage. It is likely that other cadherins have the same invasion suppressor role in carcinomas derived from other tissue types. Therefore, proteins of the present invention with cadherin activity, and polynucleotides of the present invention  
30 encoding such proteins, can be used to treat cancer. Introducing such proteins or polynucleotides into cancer cells can reduce or eliminate the cancerous changes observed in these cells by providing normal cadherin expression.

Cancer cells have also been shown to express cadherins of a different tissue type than their origin, thus allowing these cells to invade and metastasize in a different tissue in the body. Proteins of the present invention with cadherin activity, and polynucleotides of the present invention encoding such proteins, can be substituted in these cells for the  
5 inappropriately expressed cadherins, restoring normal cell adhesive properties and reducing or eliminating the tendency of the cells to metastasize.

Additionally, proteins of the present invention with cadherin activity, and polynucleotides of the present invention encoding such proteins, can be used to generate antibodies recognizing and binding to cadherins. Such antibodies can be used to block the  
10 adhesion of inappropriately expressed tumor-cell cadherins, preventing the cells from forming a tumor elsewhere. Such an anti-cadherin antibody can also be used as a marker for the grade, pathological type, and prognosis of a cancer, i.e. the more progressed the cancer, the less cadherin expression there will be, and this decrease in cadherin expression can be detected by the use of a cadherin-binding antibody.

15 Fragments of proteins of the present invention with cadherin activity, preferably a polypeptide comprising a decapeptide of the cadherin recognition site, and polynucleotides of the present invention encoding such protein fragments, can also be used to block cadherin function by binding to cadherins and preventing them from binding in ways that produce undesirable effects. Additionally, fragments of proteins of the present  
20 invention with cadherin activity, preferably truncated soluble cadherin fragments which have been found to be stable in the circulation of cancer patients, and polynucleotides encoding such protein fragments, can be used to disturb proper cell-cell adhesion.

Assays for cadherin adhesive and invasive suppressor activity include, without limitation, those described in: Hortsch et al. J Biol Chem 270 (32): 18809-18817, 1995;  
25 Miyaki et al. Oncogene 11: 2547-2552, 1995; Ozawa et al. Cell 63: 1033-1038, 1990.

#### Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities.  
30 A protein may inhibit tumor growth directly or indirectly (such as, for example, via antibody-dependent cell-mediated cytotoxicity (ADCC)). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by

inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth.

5        Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, 10 weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, 15 carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic 20 lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another 25 material or entity which is cross-reactive with such protein.

ADMINISTRATION AND DOSING

A protein of the present invention (from whatever source derived, including without limitation from recombinant and non-recombinant sources) may be used in a 30 pharmaceutical composition when combined with a pharmaceutically acceptable carrier. Such a composition may also contain (in addition to protein and a carrier) diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials well known in the art. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the

effectiveness of the biological activity of the active ingredient(s). The characteristics of the carrier will depend on the route of administration. The pharmaceutical composition of the invention may also contain cytokines, lymphokines, or other hematopoietic factors such as M-CSF, GM-CSF, TNF, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, 5 IL-13, IL-14, IL-15, IFN, TNF0, TNF1, TNF2, G-CSF, Meg-CSF, thrombopoietin, stem cell factor, and erythropoietin. The pharmaceutical composition may further contain other agents which either enhance the activity of the protein or compliment its activity or use in treatment. Such additional factors and/or agents may be included in the pharmaceutical composition to produce a synergistic effect with protein of the invention, or to minimize 10 side effects. Conversely, protein of the present invention may be included in formulations of the particular cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent to minimize side effects of the cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent.

15 A protein of the present invention may be active in multimers (e.g., heterodimers or homodimers) or complexes with itself or other proteins. As a result, pharmaceutical compositions of the invention may comprise a protein of the invention in such multimeric or complexed form.

The pharmaceutical composition of the invention may be in the form of a complex 20 of the protein(s) of present invention along with protein or peptide antigens. The protein and/or peptide antigen will deliver a stimulatory signal to both B and T lymphocytes. B lymphocytes will respond to antigen through their surface immunoglobulin receptor. T lymphocytes will respond to antigen through the T cell receptor (TCR) following presentation of the antigen by MHC proteins. MHC and structurally related proteins 25 including those encoded by class I and class II MHC genes on host cells will serve to present the peptide antigen(s) to T lymphocytes. The antigen components could also be supplied as purified MHC-peptide complexes alone or with co-stimulatory molecules that can directly signal T cells. Alternatively antibodies able to bind surface immunoglobulin and other molecules on B cells as well as antibodies able to bind the TCR and other 30 molecules on T cells can be combined with the pharmaceutical composition of the invention.

The pharmaceutical composition of the invention may be in the form of a liposome in which protein of the present invention is combined, in addition to other

pharmaceutically acceptable carriers, with amphipathic agents such as lipids which exist in aggregated form as micelles, insoluble monolayers, liquid crystals, or lamellar layers in aqueous solution. Suitable lipids for liposomal formulation include, without limitation, monoglycerides, diglycerides, sulfatides, lysolecithin, phospholipids, saponin, bile acids, and the like. Preparation of such liposomal formulations is within the level of skill in the art, as disclosed, for example, in U.S. Patent No. 4,235,871; U.S. Patent No. 4,501,728; U.S. Patent No. 4,837,028; and U.S. Patent No. 4,737,323, all of which are incorporated herein by reference.

As used herein, the term "therapeutically effective amount" means the total amount of each active component of the pharmaceutical composition or method that is sufficient to show a meaningful patient benefit, i.e., treatment, healing, prevention or amelioration of the relevant medical condition, or an increase in rate of treatment, healing, prevention or amelioration of such conditions. When applied to an individual active ingredient, administered alone, the term refers to that ingredient alone. When applied to a combination, the term refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

In practicing the method of treatment or use of the present invention, a therapeutically effective amount of protein of the present invention is administered to a mammal having a condition to be treated. Protein of the present invention may be administered in accordance with the method of the invention either alone or in combination with other therapies such as treatments employing cytokines, lymphokines or other hematopoietic factors. When co-administered with one or more cytokines, lymphokines or other hematopoietic factors, protein of the present invention may be administered either simultaneously with the cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors, or sequentially. If administered sequentially, the attending physician will decide on the appropriate sequence of administering protein of the present invention in combination with cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors.

Administration of protein of the present invention used in the pharmaceutical composition or to practice the method of the present invention can be carried out in a variety of conventional ways, such as oral ingestion, inhalation, topical application or



cutaneous, subcutaneous, intraperitoneal, parenteral or intravenous injection. Intravenous administration to the patient is preferred.

When a therapeutically effective amount of protein of the present invention is administered orally, protein of the present invention will be in the form of a tablet, capsule, powder, solution or elixir. When administered in tablet form, the pharmaceutical composition of the invention may additionally contain a solid carrier such as a gelatin or an adjuvant. The tablet, capsule, and powder contain from about 5 to 95% protein of the present invention, and preferably from about 25 to 90% protein of the present invention. When administered in liquid form, a liquid carrier such as water, petroleum, oils of animal or plant origin such as peanut oil, mineral oil, soybean oil, or sesame oil, or synthetic oils may be added. The liquid form of the pharmaceutical composition may further contain physiological saline solution, dextrose or other saccharide solution, or glycols such as ethylene glycol, propylene glycol or polyethylene glycol. When administered in liquid form, the pharmaceutical composition contains from about 0.5 to 90% by weight of protein of the present invention, and preferably from about 1 to 50% protein of the present invention.

When a therapeutically effective amount of protein of the present invention is administered by intravenous, cutaneous or subcutaneous injection, protein of the present invention will be in the form of a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such parenterally acceptable protein solutions, having due regard to pH, isotonicity, stability, and the like, is within the skill in the art. A preferred pharmaceutical composition for intravenous, cutaneous, or subcutaneous injection should contain, in addition to protein of the present invention, an isotonic vehicle such as Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, Lactated Ringer's Injection, or other vehicle as known in the art. The pharmaceutical composition of the present invention may also contain stabilizers, preservatives, buffers, antioxidants, or other additives known to those of skill in the art.

The amount of protein of the present invention in the pharmaceutical composition of the present invention will depend upon the nature and severity of the condition being treated, and on the nature of prior treatments which the patient has undergone. Ultimately, the attending physician will decide the amount of protein of the present invention with which to treat each individual patient. Initially, the attending physician will administer low doses of protein of the present invention and observe the patient's

response. Larger doses of protein of the present invention may be administered until the optimal therapeutic effect is obtained for the patient, and at that point the dosage is not increased further. It is contemplated that the various pharmaceutical compositions used to practice the method of the present invention should contain about 0.01  $\mu$ g to about 100  
5 mg (preferably about 0.1mg to about 10 mg, more preferably about 0.1  $\mu$ g to about 1 mg) of protein of the present invention per kg body weight.

The duration of intravenous therapy using the pharmaceutical composition of the present invention will vary, depending on the severity of the disease being treated and the condition and potential idiosyncratic response of each individual patient. It is  
10 contemplated that the duration of each application of the protein of the present invention will be in the range of 12 to 24 hours of continuous intravenous administration. Ultimately the attending physician will decide on the appropriate duration of intravenous therapy using the pharmaceutical composition of the present invention.

Protein of the invention may also be used to immunize animals to obtain polyclonal  
15 and monoclonal antibodies which specifically react with the protein. Such antibodies may be obtained using either the entire protein or fragments thereof as an immunogen. The peptide immunogens additionally may contain a cysteine residue at the carboxyl terminus, and are conjugated to a hapten such as keyhole limpet hemocyanin (KLH). Methods for synthesizing such peptides are known in the art, for example, as in R.P. Merrifield, J.  
20 Amer.Chem.Soc. 85, 2149-2154 (1963); J.L. Krstenansky, *et al.*, FEBS Lett. 211, 10 (1987). Monoclonal antibodies binding to the protein of the invention may be useful diagnostic agents for the immunodetection of the protein. Neutralizing monoclonal antibodies binding to the protein may also be useful therapeutics for both conditions associated with the protein and also in the treatment of some forms of cancer where abnormal expression  
25 of the protein is involved. In the case of cancerous cells or leukemic cells, neutralizing monoclonal antibodies against the protein may be useful in detecting and preventing the metastatic spread of the cancerous cells, which may be mediated by the protein.

For compositions of the present invention which are useful for bone, cartilage, tendon or ligament regeneration, the therapeutic method includes administering the  
30 composition topically, systematically, or locally as an implant or device. When administered, the therapeutic composition for use in this invention is, of course, in a pyrogen-free, physiologically acceptable form. Further, the composition may desirably be encapsulated or injected in a viscous form for delivery to the site of bone, cartilage or tissue

damage. Topical administration may be suitable for wound healing and tissue repair. Therapeutically useful agents other than a protein of the invention which may also optionally be included in the composition as described above, may alternatively or additionally, be administered simultaneously or sequentially with the composition in the  
5 methods of the invention. Preferably for bone and/or cartilage formation, the composition would include a matrix capable of delivering the protein-containing composition to the site of bone and/or cartilage damage, providing a structure for the developing bone and cartilage and optimally capable of being resorbed into the body. Such matrices may be formed of materials presently in use for other implanted medical applications.

10 The choice of matrix material is based on biocompatibility, biodegradability, mechanical properties, cosmetic appearance and interface properties. The particular application of the compositions will define the appropriate formulation. Potential matrices for the compositions may be biodegradable and chemically defined calcium sulfate, tricalciumphosphate, hydroxyapatite, polylactic acid, polyglycolic acid and  
15 polyanhydrides. Other potential materials are biodegradable and biologically well-defined, such as bone or dermal collagen. Further matrices are comprised of pure proteins or extracellular matrix components. Other potential matrices are nonbiodegradable and chemically defined, such as sintered hydroxapatite, bioglass, aluminates, or other ceramics. Matrices may be comprised of combinations of any of the above mentioned types of  
20 material, such as polylactic acid and hydroxyapatite or collagen and tricalciumphosphate. The bioceramics may be altered in composition, such as in calcium-aluminate-phosphate and processing to alter pore size, particle size, particle shape, and biodegradability.

Presently preferred is a 50:50 (mole weight) copolymer of lactic acid and glycolic acid in the form of porous particles having diameters ranging from 150 to 800 microns. In  
25 some applications, it will be useful to utilize a sequestering agent, such as carboxymethyl cellulose or autologous blood clot, to prevent the protein compositions from disassociating from the matrix.

A preferred family of sequestering agents is cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), including methylcellulose,  
30 ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, and carboxymethylcellulose, the most preferred being cationic salts of carboxymethylcellulose (CMC). Other preferred sequestering agents include hyaluronic acid, sodium alginate, poly(ethylene glycol), polyoxyethylene oxide, carboxyvinyl polymer

and poly(vinyl alcohol). The amount of sequestering agent useful herein is 0.5-20 wt%, preferably 1-10 wt% based on total formulation weight, which represents the amount necessary to prevent desorption of the protein from the polymer matrix and to provide appropriate handling of the composition, yet not so much that the progenitor cells are prevented from infiltrating the matrix, thereby providing the protein the opportunity to assist the osteogenic activity of the progenitor cells.

In further compositions, proteins of the invention may be combined with other agents beneficial to the treatment of the bone and/or cartilage defect, wound, or tissue in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factors (TGF- $\alpha$  and TGF- $\beta$ ), and insulin-like growth factor (IGF).

The therapeutic compositions are also presently valuable for veterinary applications. Particularly domestic animals and thoroughbred horses, in addition to humans, are desired patients for such treatment with proteins of the present invention.

The dosage regimen of a protein-containing pharmaceutical composition to be used in tissue regeneration will be determined by the attending physician considering various factors which modify the action of the proteins, e.g., amount of tissue weight desired to be formed, the site of damage, the condition of the damaged tissue, the size of a wound, type of damaged tissue (e.g., bone), the patient's age, sex, and diet, the severity of any infection, time of administration and other clinical factors. The dosage may vary with the type of matrix used in the reconstitution and with inclusion of other proteins in the pharmaceutical composition. For example, the addition of other known growth factors, such as IGF I (insulin like growth factor I), to the final composition, may also effect the dosage. Progress can be monitored by periodic assessment of tissue/bone growth and/or repair, for example, X-rays, histomorphometric determinations and tetracycline labeling.

Polynucleotides of the present invention can also be used for gene therapy. Such polynucleotides can be introduced either *in vivo* or *ex vivo* into cells for expression in a mammalian subject. Polynucleotides of the invention may also be administered by other known methods for introduction of nucleic acid into a cell or organism (including, without limitation, in the form of viral vectors or naked DNA).

Cells may also be cultured *ex vivo* in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced *in vivo* for therapeutic purposes.

Patent and literature references cited herein are incorporated by reference as if fully set forth.

What is claimed is:

1. An isolated polynucleotide selected from the group consisting of:
  - (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1 from nucleotide 63 to nucleotide 1265;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1 from nucleotide 132 to nucleotide 1265;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone bd306\_7 deposited with the ATCC under accession number 98599;
  - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone bd306\_7 deposited with the ATCC under accession number 98599;
  - (f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone bd306\_7 deposited with the ATCC under accession number 98599;
  - (g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone bd306\_7 deposited with the ATCC under accession number 98599;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:2;
  - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2, the fragment comprising eight consecutive amino acids of SEQ ID NO:2; and
  - (j) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i).
2. The polynucleotide of claim 1 wherein said polynucleotide is operably linked to at least one expression control sequence.
3. A host cell transformed with the polynucleotide of claim 2.
4. The host cell of claim 3, wherein said cell is a mammalian cell.

5. A process for producing a protein encoded by the polynucleotide of claim 2, which process comprises:
  - (a) growing a culture of the host cell in a suitable culture medium, wherein the host cell has been transformed with the polynucleotide of claim 2; and
  - (b) purifying said protein from the culture.
6. A protein produced according to the process of claim 5.
7. An isolated polynucleotide encoding the protein of claim 6.
8. The polynucleotide of claim 7, wherein the polynucleotide comprises the cDNA insert of clone bd306\_7 deposited with the ATCC under accession number 98599.
9. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:2;
  - (b) the amino acid sequence of SEQ ID NO:2 from amino acid 148 to amino acid 189;
  - (c) fragments of the amino acid sequence of SEQ ID NO:2 comprising eight consecutive amino acids of SEQ ID NO:2; and
  - (d) the amino acid sequence encoded by the cDNA insert of clone bd306\_7 deposited with the ATCC under accession number 98599;the protein being substantially free from other mammalian proteins.
10. The protein of claim 9, wherein said protein comprises the amino acid sequence of SEQ ID NO:2.
11. The protein of claim 9, wherein said protein comprises the amino acid sequence of SEQ ID NO:2 from amino acid 148 to amino acid 189.
12. A composition comprising the protein of claim 9 and a pharmaceutically acceptable carrier.

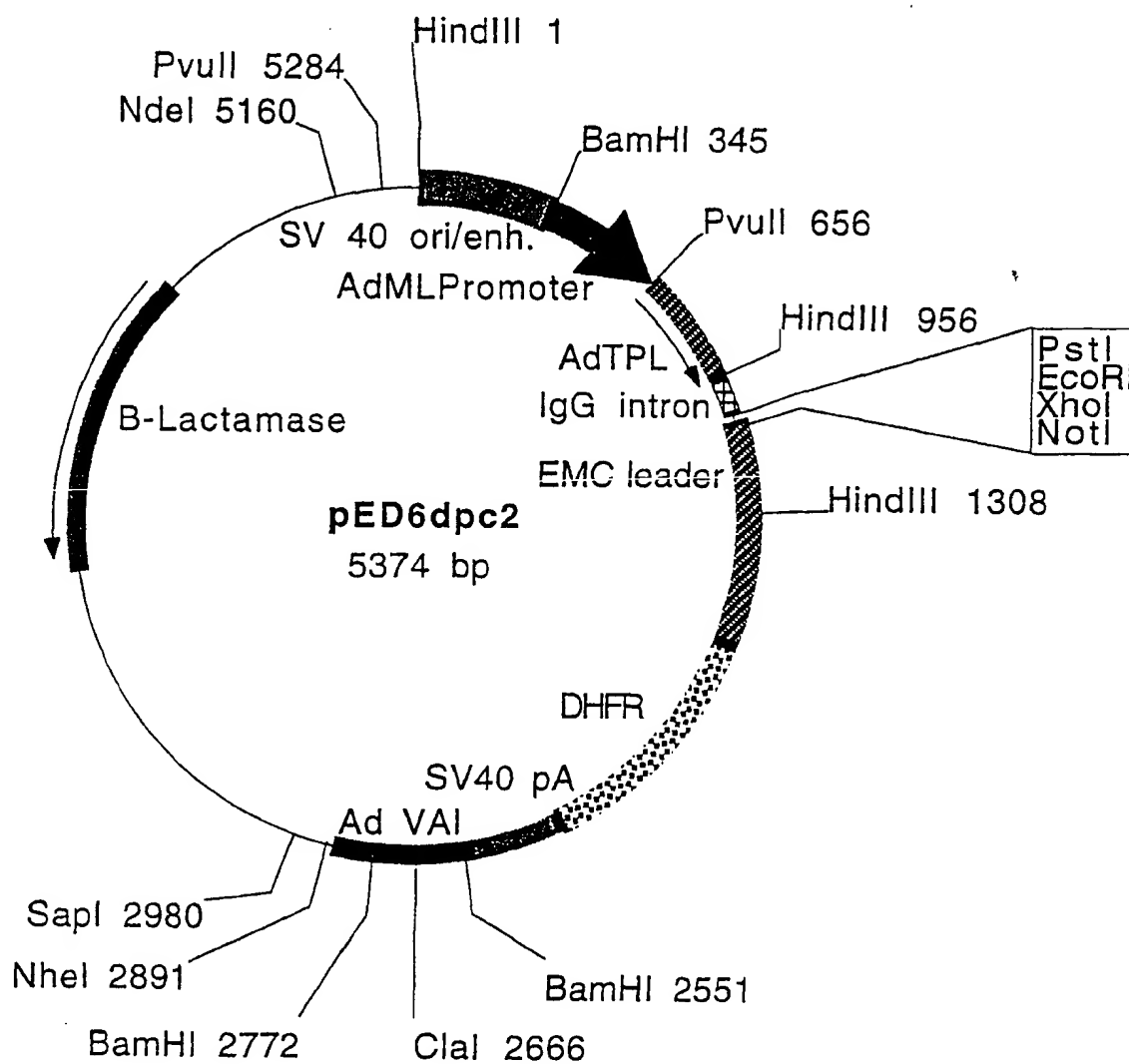
13. An isolated polynucleotide selected from the group consisting of:
- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19 from nucleotide 27 to nucleotide 734;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19 from nucleotide 270 to nucleotide 734;
  - (d) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19 from nucleotide 85 to nucleotide 1604;
  - (e) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone yb8\_1 deposited under accession number ATCC 98599;
  - (f) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone yb8\_1 deposited under accession number ATCC 98599;
  - (g) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone yb8\_1 deposited under accession number ATCC 98599;
  - (h) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone yb8\_1 deposited under accession number ATCC 98599;
  - (i) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:20;
  - (j) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:20, the fragment comprising eight consecutive amino acids of SEQ ID NO:20; and
  - (k) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(j).
14. A protein comprising an amino acid sequence selected from the group consisting of:
- (a) the amino acid sequence of SEQ ID NO:20;
  - (b) the amino acid sequence of SEQ ID NO:20 from amino acid 70 to amino acid 236;



(c) fragments of the amino acid sequence of SEQ ID NO:20 comprising eight consecutive amino acids of SEQ ID NO:20; and

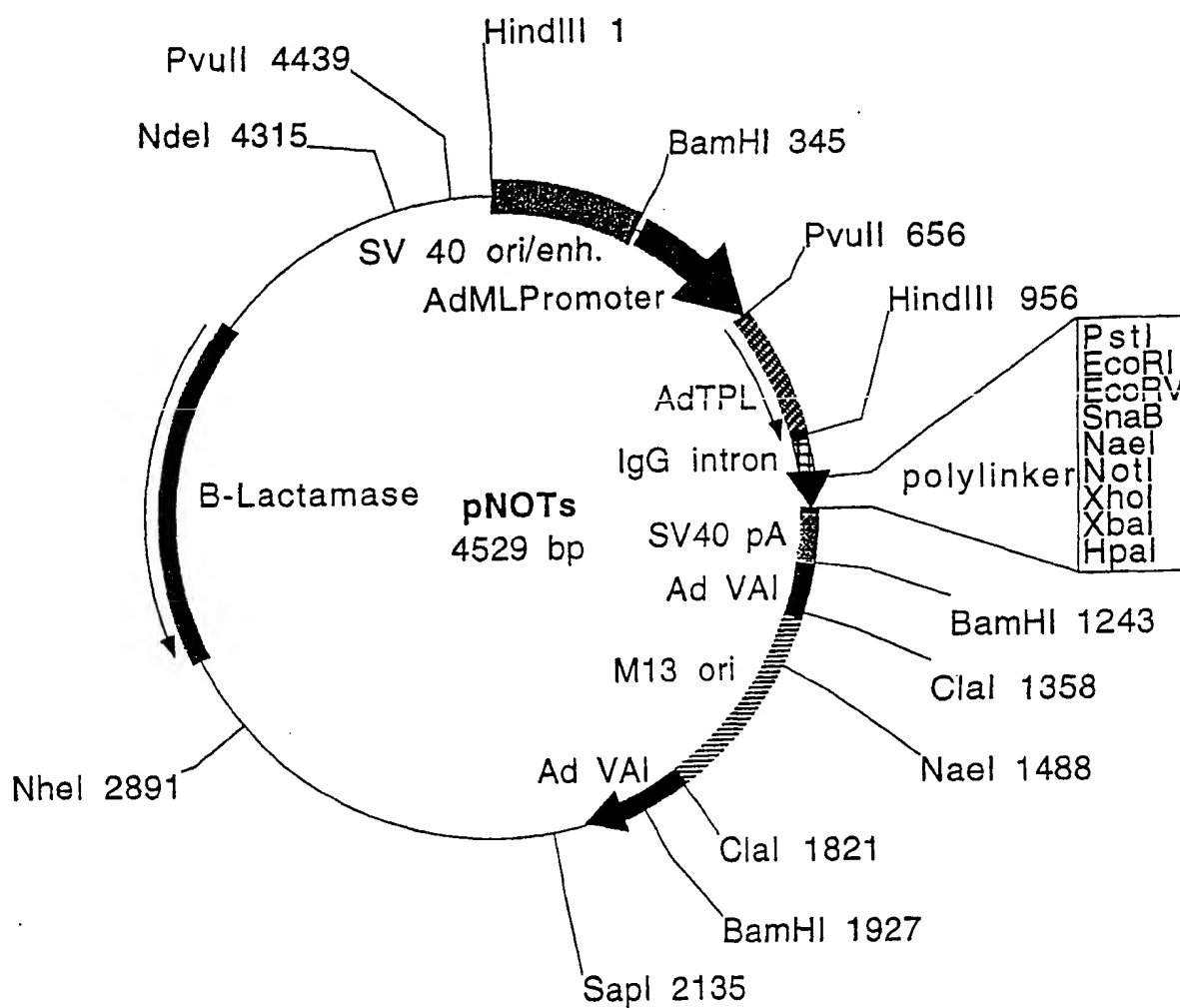
(d) the amino acid sequence encoded by the cDNA insert of clone yb8\_1 deposited under accession number ATCC 98599;

the protein being substantially free from other mammalian proteins.

Fig. 1A<sup>1/2</sup>

2/2

Fig. 1B



1.

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 Asn Glu Pro Thr Gln Asn Gln Phe Gly Glu Gly Ser Leu Phe Phe Phe  
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 Leu Lys Glu Phe Gln Val Cys Ala Asp Lys Val Leu Gly Ile Glu Ser  
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 His His Asp Phe Leu Val Lys Val Lys Val Gly Lys Phe Met Ala Lys  
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 <213> Homo sapiens

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 <212> PRT  
 <213> Homo sapiens

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 Gln Val Leu Leu Phe Pro Phe Leu Asn Tyr Tyr Leu Leu Leu Leu Phe  
 35 40 45  
 Phe Glu Thr Gly Ser Pro Phe Val Thr Gln Ala Gly Met Gln Arg His  
 50 55 60  
 Asp His Cys Ser Leu Gln Leu Arg Pro Pro Arg Leu Lys Gly Val Ser  
 65 70 75 80  
 His Leu Gly Cys Cys His Thr Trp Pro Thr Phe Leu Tyr Phe Phe Gly  
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 <212> DNA  
 <213> Homo sapiens

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 Leu Phe Leu Ala Ser Ala Val Leu Ser Trp Lys Leu Ala Lys Met Ile  
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 <211> 819  
 <212> DNA  
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 <211> 89  
 <212> PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 10

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Cys Cys Cys Ala Leu Asn Ser Val Pro Ala Val Ser Gly Arg Leu Glu  
 35 40 45

Lys Lys Ile Pro Pro Leu Lys Thr Cys Ser Leu Phe Phe Gln Ser Val  
 50 55 60

Thr Pro Ala Ile Ser Leu Ala Ser His Gly Ser Val Asn Trp His Thr  
 65 70 75 80

Ala Ala Val Arg Gln Trp Lys Lys Ser  
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&lt;210&gt; 11

&lt;211&gt; 1969

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 11

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10

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 <211> 211  
 <212> PRT  
 <213> Homo sapiens

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 Leu His His Tyr Phe Val Pro Asp Gly Asp Tyr Glu Glu Asn Asp Asp  
 35 40 45  
 Pro Glu Lys Cys Gln Leu Leu Phe Arg Val Ser Asp His Arg Arg Cys  
 50 55 60  
 Ser Gln Gly Glu Gly Ser Gln Val Gly Ser Leu Leu Ser Leu Thr Leu  
 65 70 75 80  
 Arg Glu Glu Phe Thr Val Leu Gly Arg Gln Val Glu Asp Ala Gly Arg  
 85 90 95  
 Val Leu Glu Gly Ile Ser Lys Ser Ile Ser Tyr Asp Leu Asp Gly Glu  
 100 105 110  
 Glu Ser Tyr Gly Lys Tyr Leu Arg Arg Glu Ser His Gln Ile Gly Asp  
 115 120 125  
 Ala Tyr Ser Asn Ser Asp Lys Ser Leu Thr Glu Leu Glu Ser Lys Phe  
 130 135 140  
 Lys Gln Gly Gln Glu Gln Asp Ser Arg Gln Glu Ser Arg Leu Asn Glu  
 145 150 155 160  
 Asp Phe Leu Gly Met Leu Val His Thr Arg Ser Leu Leu Lys Glu Thr  
 165 170 175  
 Leu Asp Ile Ser Val Gly Leu Arg Asp Lys Tyr Glu Leu Leu Ala Leu  
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<210> 13  
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 <212> DNA  
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11.

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     20                    25                    30

Pro Met Phe Gly Asp Tyr Glu Ala Gln Arg His Trp Gln Glu Ile Thr  
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 85 90 95  
 Leu His Thr Ser Arg Gly Tyr Glu Ser Gln Ala His Lys Leu Phe Met  
 100 105 110  
 Arg Thr Thr Val Leu Ile Ala Asp Leu Leu Ile Tyr Ile Pro Ala Val  
 115 120 125  
 Val Leu Tyr Cys Cys Cys Leu Lys Glu Ile Ser Thr Lys Lys Lys Ile  
 130 135 140  
 Ala Asn Ala Leu Cys Ile Leu Leu Tyr Pro Gly Leu Ile Leu Ile Asp  
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 Tyr Gly His Phe Gln Tyr Asn Ser Val Ser Leu Gly Phe Ala Leu Trp  
 165 170 175  
 Gly Val Leu Gly Ile Ser Cys Asp Cys Asp Leu Leu Gly Ser Leu Ala  
 180 185 190  
 Phe Cys Leu Ala Ile Asn Tyr Lys Gln Met Glu Leu Tyr His Ala Leu  
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 Pro Phe Phe Cys Phe Leu Leu Gly Lys Cys Phe Lys Lys Gly Leu Lys  
 210 215 220  
 Gly Lys Gly Phe Val Xaa Leu Val Lys Leu Ala Xaa Ile Val Val Ala  
 225 230 235 240  
 Ser Phe Val Leu Cys Trp Leu Pro Phe Phe Thr Glu Arg Glu Gln Thr  
 245 250 255  
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 260 265 270  
 Asp Lys Val Ala Asn Ile Trp Cys Ser Phe Asn Val Phe Leu Lys Ile  
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 Thr Phe Leu Ser Leu Leu Pro Ala Cys Ile Lys Leu Ile Leu Gln Pro  
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 Ser Ser Lys Gly Phe Lys Phe Thr Leu Val Ser Cys Ala Leu Ser Phe  
 325 330 335  
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 340 345 350  
 Leu Pro Val Cys Leu Val Leu Ser Glu Ile Pro Phe Met Ser Thr Trp  
 355 360 365

Phe Leu Leu Val Ser Thr Phe Ser Met Leu Pro Leu Leu Leu Lys Asp  
 370 375 380  
 Glu Leu Leu Met Pro Ser Val Val Thr Thr Met Ala Phe Phe Ile Ala  
 385 390 395 400  
 Cys Val Thr Ser Phe Ser Ile Phe Glu Lys Thr Ser Glu Glu Glu Leu  
 405 410 415  
 Gln Leu Lys Ser Phe Ser Ile Ser Val Arg Lys Tyr Leu Pro Cys Xaa  
 420 425 430  
 Thr Phe Leu Ser Arg Ile Xaa Gln Tyr Leu Phe Leu Ile Ser Val Ile  
 435 440 445  
 Thr Met Val Leu Leu Thr Leu Met Thr Val Thr Leu Asp Pro Pro Gln  
 450 455 460  
 Lys Leu Pro Asp Leu Phe Ser Val Leu Val Cys Xaa Val Ser Cys Leu  
 465 470 475 480  
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14

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Val Leu Phe Asn Ile Ile Ile Ile Phe Leu Met Phe Phe Asn Thr Phe  
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Val Phe Gln Ala Gly Leu Val Asn Leu Leu Phe His Lys Phe Lys Gly  
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Thr Ile Ile Leu Thr Ala Val Tyr Phe Ala Leu Ser Ile Ser Leu His  
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Val Trp Val Met Asn Leu Arg Trp Lys Asn Ser Asn Ser Phe Ile Trp  
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<211> 1348

<212> DNA

<213> Homo sapiens

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<212> PRT

<213> Homo sapiens

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 Arg Phe Lys Asp Trp Leu Gln Asp Gly Asn His Leu Phe Arg Ile Leu  
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 Gly Leu Arg Gly Leu Tyr Asn Leu Val Gly His Gln Glu Met Arg Glu  
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 Asp Ile Lys Ser Leu Leu Pro Tyr Ile Val Asp Ser Leu Arg Glu Thr  
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 Asp Glu Lys Ile Val Leu Ser Ala Ile Gln Ile Leu Leu Gln Leu Val  
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 Arg Thr Met Asp Phe Thr Thr Leu Ala Ala Met Met Arg Thr Leu Phe  
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 Ser Leu Phe Gly Asp Val Arg Ser Asp Val His Arg Phe Ser Val Thr  
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 Leu Phe Gly Ala Ala Ile Lys Ser Val Lys Asn Pro Asp Lys Lys Ser  
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 Ile Glu Asn Gln Val Leu Asp Ser Leu Val Pro Leu Leu Leu Tyr Ser  
 195 200 205  
 Gln Asp Glu Asn Asp Ala Val Ala Glu Glu Ser Arg Gln Val Leu Thr  
 210 215 220  
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 225 230 235 240  
 Lys Asp Pro Trp His Ile Lys Pro Thr Glu Ala Gly Thr Ile Cys Arg  
 245 250 255  
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 Arg Met Gly Thr Asp Trp Ile Glu Asp Asp Leu Arg Asp Leu Leu Cys  
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 Asp Pro Glu Pro Ser Leu Cys Ile Ile Ala Ser Gln Thr Leu Leu Leu  
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 <212> PRT  
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17

Gly Thr Thr Leu Ile Met Leu Leu Ser Leu Ala Ala Phe Ser Val Ile  
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Phe Arg Ile Tyr Lys Ser Val Ile Gln Ala Val Gln Lys Ser Glu Glu  
100 105 110

Gly His Pro Phe Lys Ala Tyr Leu Asp Val Asp Ile Thr Leu Ser Ser  
115 120 125

Glu Ala Phe His Asn Tyr Met Asn Ala Ala Met Val His Ile Asn Arg  
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Ala Leu Lys Leu Ile Ile Arg Leu Phe Leu Val Glu Asp Leu Val Asp  
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Val Phe Asn Gly Ile Thr Leu Leu Ile Leu Ala Glu Leu Leu Ile Phe  
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Ser Val Pro Ile Val Tyr Glu Lys Tyr Lys Thr Gln Ile Asp His Tyr  
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Ala Lys Leu Pro Gly Ile Ala Lys Lys Lys Ala Glu  
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&lt;210&gt; 21

&lt;211&gt; 2439

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 21

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&lt;210&gt; 22

&lt;211&gt; 47

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 22

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Leu Ser Phe Trp Ile Val Ile Ile Tyr Leu Ile Ala Cys Leu Ser Ala
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&lt;210&gt; 23

&lt;211&gt; 1132

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (1009)

&lt;400&gt; 23

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19

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 Met Tyr Phe Ser Pro Leu Tyr Phe Ile Ile Phe Leu Lys Ser Ser Asn  
 35 40 45  
 Leu Asn Thr Trp Thr Ser Tyr Trp Ile Thr Leu Ile His Ile Phe Ile  
 50 55 60  
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Ser Lys

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 <213> Homo sapiens

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 <211> 38  
 <212> PRT  
 <213> Homo sapiens

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 Met Phe Glu Ile Gln Glu  
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 <212> DNA  
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 <211> 86  
 <212> PRT  
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 20 25 30  
 Lys Phe Leu Glu Val Arg Phe Pro Gly Gln Arg Leu Asn Ala His Val  
 35 40 45  
 Ile Leu Leu Asp Ile Val Lys Ser Pro Tyr Arg Ala Cys Thr Thr Gln  
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21

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 <213> Homo sapiens

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           20                    25                    30  
 Thr Gly Ser Ser Val Ile Ser Ser Gly Ala Ser Thr Ala Thr Asn Ser  
       35                    40                    45  
 Gly Ser Ser Val Thr Ser Ser Gly Val Ser Thr Ala Thr Ile Ser Gly  
       50                    55                    60  
 Ser Ser Val Thr Ser Asn Gly Val Ser Ile Val Thr Asn Ser Glu Phe  
       65                    70                    75                    80  
 His Thr Thr Ser Ser Gly Ile Ser Thr Ala Thr Asn Ser Glu Phe Ser  
           85                    90                    95  
 Thr Ala Ser Ser Gly Ile Ser Ile Ala Thr Asn Ser Glu Ser Ser Thr  
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 Thr Ser Ser Gly Ala Ser Thr Ala Thr Asn Ser Glu Ser Ser Thr Pro  
       115                    120                    125  
 Ser Ser Gly Ala Ser Thr Ala Thr Asn Ser Asp Ser Ser Thr Thr Ser  
       130                    135                    140  
 Ser Gly Ala Ser Thr Ala Thr Asn Ser Asp Ser Ser Leu Gly Asn Lys  
       145                    150                    155                    160  
 Ser Gly Thr Leu Phe Gln Lys Arg Lys Lys Glu Ile Gln Leu Pro Leu  
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 Lys Val Gln Leu Tyr Ser Val Ile Asp Lys  
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 <212> DNA  
 <213> Homo sapiens

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&lt;210&gt; 32

&lt;211&gt; 184

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 32

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Met Phe Ile Phe Leu Leu Leu Leu Val Leu Leu Gly Ser Tyr Ala Arg
      20             25             30

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Ser Asp Thr Thr Leu Lys Pro Arg Pro Val Ser Trp Ser Phe Ser Pro
    35             40             45

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Val Phe Ser Ser Thr Gly Phe Thr Val Ser Gly Leu Thr Ile Lys Pro  
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Leu Ser Ile Leu Asn Gly Phe Leu Cys Arg Asp Ile Pro Ser Thr Arg  
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Ala Ser Ser Gly Leu Ala Asp Ala Pro Pro Ser Pro Leu Cys Pro Leu  
85 90 95

His Ser Thr Leu Phe Met Trp Lys Asn Pro Trp His Pro Arg Val Ala  
100 105 110

Ser Leu Ser Tyr Pro Ala Pro His Gly Asp Leu Thr Leu Ala Ser Leu  
115 120 125

Thr Trp Val Ser Leu Pro Asn Pro Leu Pro Gly Pro Thr Thr Ala Ser  
130 135 140

Ile Pro Asp Leu Pro Arg Gly Pro Ile Pro Ala Val Leu Arg His Leu  
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Lys Glu Ser Cys Arg Leu Phe Leu  
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<210> 33

<211> 1819

<212> DNA

<213> Homo sapiens

<400> 33

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 <212> PRT  
 <213> Homo sapiens

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 Arg Ile Lys Ala Pro Ser Gly Gln Ser Ile Arg Asn Thr Glu Asn Lys  
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 Glu Asn Ile Val Asn Thr Arg Phe Glu Gly Ile Lys Cys Leu Tyr Ile  
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<210> 35  
 <211> 1269  
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 <211> 100  
 <212> PRT  
 <213> Homo sapiens

<400> 36

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 Leu Trp Ile Tyr His Ser Lys Asn Pro Glu Val Asp Asp Ser Ser Ala  
 35 40 45  
 Gln Lys Gly Trp Trp Phe Leu Ser Trp Phe Asn Asn Gly Ile His Asn  
 50 55 60  
 Tyr Gln Gln Gly Glu Glu Asp Ile Asp Lys Glu Lys Gly Arg Glu Glu  
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 <211> 232  
 <212> DNA  
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<210> 38  
 <211> 57  
 <212> PRT  
 <213> Homo sapiens

<400> 38  
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<210> 39  
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 <212> DNA  
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&lt;210&gt; 40

&lt;211&gt; 54

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 40

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Met Lys Phe Gln Leu Leu Asn Leu Leu Pro Tyr Pro Gly Leu Trp Thr
  1             5             10             15

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Gln Thr Gly Leu Glu Pro Gln Ser Leu Phe Pro Ser Ser Pro Ser Ser
      20             25             30

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Pro Cys Gly Leu Pro Gly Leu Ser Ile Cys Tyr Cys Ala Val Leu Gly
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Ile Gly Ala Glu Val Ala
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&lt;210&gt; 41

&lt;211&gt; 4292

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 41

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tgagaatcag aagcttcaac agaaacttaa agtaatgact gaattatatc aagaaaatga 3180
aatgaaactc caccggaaat taacagtaga ggaaaattat cggttagaga aagaagagaa 3240
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acatccagaa ccacagcaag aaacctgaca at

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&lt;210&gt; 42

&lt;211&gt; 1369

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 42

Met Ala Lys Phe Gly Val His Arg Ile Leu Leu Leu Ala Ile Ser Leu

1

5

10

15

Thr Lys Cys Leu Glu Ser Thr Lys Leu Leu Ala Asp Leu Lys Lys Cys  
 20 25 30  
 Gly Asp Leu Glu Cys Glu Ala Leu Ile Asn Arg Val Ser Ala Met Arg  
 35 40 45  
 Asp Tyr Arg Gly Pro Asp Cys Arg Tyr Leu Asn Phe Thr Lys Gly Glu  
 50 55 60  
 Glu Ile Ser Val Tyr Val Lys Leu Ala Gly Glu Arg Glu Asp Leu Trp  
 65 70 75 80  
 Ala Gly Ser Lys Gly Lys Glu Phe Gly Tyr Phe Pro Arg Asp Ala Val  
 85 90 95  
 Gln Ile Glu Glu Val Phe Ile Ser Glu Glu Ile Gln Met Ser Thr Lys  
 100 105 110  
 Glu Ser Asp Phe Leu Cys Leu Leu Gly Val Ser Tyr Thr Phe Asp Asn  
 115 120 125  
 Glu Asp Ser Glu Leu Asn Gly Asp Tyr Gly Glu Asn Ile Tyr Pro Tyr  
 130 135 140  
 Glu Glu Asp Lys Asp Glu Lys Ser Ser Ile Tyr Glu Ser Asp Phe Gln  
 145 150 155 160  
 Ile Glu Pro Gly Phe Tyr Ala Thr Tyr Glu Ser Thr Leu Phe Glu Asp  
 165 170 175  
 Gln Val Pro Ala Leu Glu Ala Pro Glu Asp Ile Gly Ser Thr Ser Glu  
 180 185 190  
 Ser Lys Asp Trp Glu Glu Val Val Val Glu Ser Met Glu Gln Asp Arg  
 195 200 205  
 Ile Pro Glu Val His Val Pro Pro Ser Ser Ala Val Ser Gly Val Lys  
 210 215 220  
 Glu Trp Phe Gly Leu Gly Gly Glu Gln Ala Glu Glu Lys Ala Phe Glu  
 225 230 235 240  
 Ser Val Ile Glu Pro Val Gln Glu Ser Ser Phe Arg Ser Arg Lys Ile  
 245 250 255  
 Ala Val Glu Asp Glu Asn Asp Leu Glu Glu Leu Asn Asn Gly Glu Pro  
 260 265 270  
 Gln Thr Glu His Gln Gln Glu Ser Glu Ser Glu Ile Asp Ser Val Pro  
 275 280 285  
 Lys Thr Gln Ser Glu Leu Ala Ser Glu Ser Glu His Ile Pro Lys Pro  
 290 295 300  
 Gln Ser Thr Gly Trp Phe Gly Gly Gly Phe Thr Ser Tyr Leu Gly Phe  
 305 310 315 320  
 Gly Asp Glu Asp Thr Gly Leu Glu Leu Ile Ala Glu Glu Ser Asn Pro  
 325 330 335  
 Pro Leu Gln Asp Phe Pro Asn Pro Ile Ser Ser Asp Lys Glu Ala Thr  
 340 345 350

29.

Val Pro Cys Thr Glu Ile Leu Thr Glu Lys Lys Asp Thr Ile Thr Asn  
 355 360 365  
 Asp Ser Leu Ser Leu Lys Pro Ser Trp Phe Asp Phe Gly Phe Ala Ile  
 370 375 380  
 Leu Gly Phe Ala Tyr Ala Lys Glu Asp Lys Ile Met Leu Asp Asp Arg  
 385 390 395 400  
 Lys Asn Glu Glu Asp Gly Gly Ala Asp Glu His Glu His Pro Leu Thr  
 405 410 415  
 Ser Glu Leu Asp Pro Glu Lys Glu Gln Glu Ile Glu Thr Ile Lys Ile  
 420 425 430  
 Ile Glu Thr Glu Asp Gln Ile Asp Lys Lys Pro Val Ser Glu Lys Thr  
 435 440 445  
 Asp Glu Ser Asp Thr Ile Pro Tyr Leu Lys Lys Phe Leu Tyr Asn Phe  
 450 455 460  
 Asp Asn Pro Trp Asn Phe Gln Asn Ile Pro Lys Glu Thr Glu Leu Pro  
 465 470 475 480  
 Phe Pro Lys Gln Ile Leu Asp Gln Asn Asn Val Ile Glu Asn Glu Glu  
 485 490 495  
 Thr Gly Glu Phe Ser Ile Asp Asn Tyr Pro Thr Asp Asn Thr Lys Val  
 500 505 510  
 Met Ile Phe Lys Ser Ser Tyr Ser Leu Ser Asp Met Val Ser Asn Ile  
 515 520 525  
 Glu Leu Pro Thr Arg Ile His Glu Glu Val Tyr Phe Glu Pro Ser Ser  
 530 535 540  
 Ser Lys Asp Ser Asp Glu Asn Ser Lys Pro Ser Val Asp Thr Glu Gly  
 545 550 555 560  
 Pro Ala Leu Val Glu Ile Asp Arg Ser Val Glu Asn Thr Leu Leu Asn  
 565 570 575  
 Ser Gln Met Val Ser Thr Asp Asn Ser Leu Ser Ser Gln Asn Tyr Ile  
 580 585 590  
 Ser Gln Lys Glu Asp Ala Ser Glu Phe Gln Ile Leu Lys Tyr Leu Phe  
 595 600 605  
 Gln Ile Asp Val Tyr Asp Phe Met Asn Ser Ala Phe Ser Pro Ile Val  
 610 615 620  
 Ile Leu Thr Glu Arg Val Val Ala Ala Leu Pro Glu Gly Met Arg Pro  
 625 630 635 640  
 Asp Ser Asn Leu Tyr Gly Phe Pro Trp Glu Leu Val Ile Cys Ala Ala  
 645 650 655  
 Val Val Gly Phe Phe Ala Val Leu Phe Phe Leu Trp Arg Ser Phe Arg  
 660 665 670



30.

Ser Val Arg Ser Arg Leu Tyr Val Gly Arg Glu Lys Lys Leu Ala Leu  
 675 680 685  
 Met Leu Ser Gly Leu Ile Glu Glu Lys Ser Lys Leu Leu Glu Lys Phe  
 690 695 700  
 Ser Leu Val Gln Lys Glu Tyr Glu Gly Tyr Glu Val Glu Ser Ser Leu  
 705 710 715 720  
 Lys Asp Ala Ser Phe Glu Lys Glu Ala Thr Glu Ala Gln Ser Leu Glu  
 725 730 735  
 Ala Thr Cys Glu Lys Leu Asn Arg Ser Asn Ser Glu Leu Glu Asp Glu  
 740 745 750  
 Ile Leu Cys Leu Glu Lys Glu Leu Lys Glu Glu Lys Ser Lys His Ser  
 755 760 765  
 Glu Gln Asp Glu Leu Met Ala Asp Ile Ser Lys Arg Ile Gln Ser Leu  
 770 775 780  
 Glu Asp Glu Ser Lys Ser Leu Lys Ser Gln Val Ala Glu Ala Lys Met  
 785 790 795 800  
 Thr Phe Lys Ile Phe Gln Met Asn Glu Glu Arg Leu Lys Ile Ala Ile  
 805 810 815  
 Lys Asp Ala Leu Asn Glu Asn Ser Gln Leu Gln Glu Ser Gln Lys Gln  
 820 825 830  
 Leu Leu Gln Glu Ala Glu Val Trp Lys Glu Gln Val Ser Glu Leu Asn  
 835 840 845  
 Lys Gln Lys Val Thr Phe Glu Asp Ser Lys Val His Ala Glu Gln Val  
 850 855 860  
 Leu Asn Asp Lys Glu Ser His Ile Lys Thr Leu Thr Glu Arg Leu Leu  
 865 870 875 880  
 Lys Met Lys Asp Trp Ala Ala Met Leu Gly Glu Asp Ile Thr Asp Asp  
 885 890 895  
 Asp Asn Leu Glu Leu Glu Met Asn Ser Glu Ser Glu Asn Gly Ala Tyr  
 900 905 910  
 Leu Asp Asn Pro Pro Lys Gly Ala Leu Lys Lys Leu Ile His Ala Ala  
 915 920 925  
 Lys Leu Asn Ala Ser Leu Lys Thr Leu Glu Gly Glu Arg Asn Gln Ile  
 930 935 940  
 Tyr Ile Gln Leu Ser Glu Val Asp Lys Thr Lys Glu Glu Leu Thr Glu  
 945 950 955 960  
 His Ile Lys Asn Leu Gln Thr Gln Gln Ala Ser Leu Gln Ser Glu Asn  
 965 970 975  
 Thr His Phe Glu Asn Glu Asn Gln Lys Leu Gln Gln Lys Leu Lys Val  
 980 985 990  
 Met Thr Glu Leu Tyr Gln Glu Asn Glu Met Lys Leu His Arg Lys Leu  
 995 1000 1005

Thr Val Glu Glu Asn Tyr Arg Leu Glu Lys Glu Glu Lys Leu Ser Lys  
 1010 1015 1020  
 Val Asp Glu Lys Ile Ser His Ala Thr Glu Glu Leu Glu Thr Tyr Arg  
 1025 1030 1035 1040  
 Lys Arg Ala Lys Asp Leu Glu Glu Glu Leu Glu Arg Thr Ile His Ser  
 1045 1050 1055  
 Tyr Gln Gly Gln Ile Ile Ser His Glu Lys Lys Ala His Asp Asn Trp  
 1060 1065 1070  
 Leu Ala Ala Arg Asn Ala Glu Arg Asn Leu Asn Asp Leu Arg Lys Glu  
 1075 1080 1085  
 Asn Ala His Asn Arg Gln Lys Leu Thr Glu Thr Glu Leu Lys Phe Glu  
 1090 1095 1100  
 Leu Leu Glu Lys Asp Pro Tyr Ala Leu Asp Val Pro Asn Thr Ala Phe  
 1105 1110 1115 1120  
 Gly Arg Gly Ser Arg Gly Pro Gly Asn Pro Leu Asp His Gln Ile Thr  
 1125 1130 1135  
 Asn Glu Arg Gly Glu Ser Ser Cys Asp Arg Leu Thr Asp Pro His Arg  
 1140 1145 1150  
 Ala Pro Ser Asp Thr Gly Ser Leu Ser Pro Pro Trp Asp Gln Asp Arg  
 1155 1160 1165  
 Arg Met Met Phe Pro Pro Gly Gln Ser Tyr Pro Asp Ser Ala Leu  
 1170 1175 1180  
 Pro Pro Gln Arg Gln Asp Arg Phe Cys Ser Asn Ser Gly Arg Leu Ser  
 1185 1190 1195 1200  
 Gly Pro Ala Glu Leu Arg Ser Phe Asn Met Pro Ser Leu Asp Lys Met  
 1205 1210 1215  
 Asp Gly Ser Met Pro Ser Glu Met Glu Ser Ser Arg Asn Asp Thr Lys  
 1220 1225 1230  
 Asp Asp Leu Gly Asn Leu Asn Val Pro Asp Ser Ser Leu Pro Ala Glu  
 1235 1240 1245  
 Asn Glu Ala Thr Gly Pro Gly Phe Val Pro Pro Pro Leu Ala Pro Ile  
 1250 1255 1260  
 Arg Gly Pro Leu Phe Pro Val Asp Ala Arg Gly Pro Phe Leu Arg Arg  
 1265 1270 1275 1280  
 Gly Pro Pro Phe Pro Pro Pro Pro Pro Gly Ala Met Phe Gly Ala Ser  
 1285 1290 1295  
 Arg Asp Tyr Phe Pro Pro Arg Asp Phe Pro Gly Pro Pro Pro Ala Pro  
 1300 1305 1310  
 Phe Ala Met Arg Asn Val Tyr Pro Pro Arg Gly Phe Pro Pro Tyr Leu  
 1315 1320 1325

32,

Pro Pro Arg Pro Gly Phe Phe Pro Pro Pro Pro His Ser Glu Gly Arg  
1330 1335 1340

Ser Glu Phe Pro Ser Gly Leu Ile Pro Pro Ser Asn Glu Pro Ala Thr  
1345 1350 1355 1360

Glu His Pro Glu Pro Gln Gln Glu Thr  
1365

<210> 43  
<211> 412  
<212> DNA  
<213> Homo sapiens

<400> 43  
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tgggcccggc aagagcactc atggggccgg attcacgccc cgggcccgtt ccctcctgct 180  
ctctggtgct cctcacgcca ttggccccac tgcctctcac tgcccgtgag tcctctgtgcc 240  
cgtgtcctcc ttcttgaacc cctcagccct cagttaacct tcagaaagct ggctcggaga 300  
agtccttggg tgggtatctg gaggcagagt ttgccgtgag ccgagattgt gccactgcac 360  
gcactccagc ctgggcgaca gagcgagacc ccatctcaaa aaaaaaaaaa aa 412

<210> 44  
<211> 49  
<212> PRT  
<213> Homo sapiens

<400> 44  
Met Gly Pro Val Leu Gly Gly Arg Arg Ala Leu Met Gly Pro Asp Ser  
1 5 10 15

Arg Pro Gly Pro Val Pro Ser Cys Ser Leu Val Leu Leu Thr Pro Leu  
20 25 30

Ala Pro Leu Pro Leu Thr Ala Arg Glu Ser Leu Cys Pro Cys Pro Pro  
35 40 45

Ser

<210> 45  
<211> 1317  
<212> DNA  
<213> Homo sapiens

<400> 45  
gtctgtgaga gtcaattcag gggaaagata caagattgat ttgtaaaacc cttgaaatgt 60  
agatttcttg tagatgtatc ctacacgttg taaatatgtt ttgtagagtg aagccatggg 120  
aagccatgtg taacagagct tagacatcca aaactaatca atgctgaggt ggctaaatac 180  
ctagcctttt acatgtaaac ctgtctgcaa aattagcttt tttaaaaaaaa aaaaaaaaaa 240  
aaaattgggg ggggttaattt atcattcaga aatcttgcat tttcaaaaat tcagtgcag 300  
cgccaggcga tttgtgtcta aggatacgat tttgaaccat atgggcagtg tacaaaaat 360  
gaaacaactg tttccacact tgcacctgat caagagcagt gcttctccat ttgttttgca 420  
gagaaatgtt tttcatttcc cgtgtgtttc catttccttc tgaaattctg attttatcca 480  
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gtttgtataa attattgaaa tccatttgca ccctgtaaga atggacttaa aagtactgct 660  
ggacaggcat gtgtgtctca agtacattga ttgctcaaat ataaggaaat ggcccaatga 720  
acgtggttgt gggaggggaa agaggaaaca gagctagtca gatgtgaatt gtatctgttg 780

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taataaacat gttaaaacaa acaaaaattg ttatTTTTct tttccttcgg tcagtgcaca 840
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taattgaaat aattccttaa gggaggTTTT gtttaaaacg tattaacagg aaattgtgta 960
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tttTgtTgt agctaactgt tcaagtctgg tgctgactgc tgttcttagc catcacaaaa 1140
cgctaaattt gtgtaattgg agcttcctgc tgttatctgg aaatagcagg aaagcgcagc 1200
tttTtatatt gtttcctaaa gtatattaaa ataaaaaaag aaactattgc tactaaaaaa 1260
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa 1317

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&lt;210&gt; 46

&lt;211&gt; 48

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 46

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Met Phe Phe Ile Ser Arg Val Phe Pro Phe Pro Ser Glu Ile Leu Ile
  1             5             10             15

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Leu Ser Ile Phe Leu Arg Leu Leu Phe Ile Ser Phe Leu Lys Ala Leu
      20             25             30

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Leu Leu Trp His Phe Ser Ile Thr Phe Ser Phe Leu Cys Thr Val Ala
  35             40             45

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&lt;210&gt; 47

&lt;211&gt; 1442

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 47

```

tgcggtTgtt ttccttctct ccgtgcaacg ctggcaagtc tcaaagtcgc cacagaaaca 60
tgccccctgat tcagtgcctc tgcttagctg taacatgtta atcagaacta cctggcatct 120
tccTgaacaa gactttcaat aggggccagt atgcttcgct tcatccagaa gttttctcaa 180
gcatcttcaa agatactgaa gtactcttcc ccagtgggac taagaaccag cagaacagat 240
atactttctc tcaagatgtc tctccagcaa aacttttccc catgtccaag gccttggctt 300
tctcatcat ttcacgcgta tatgagcaag acacagtgtc atcacatc cccctgcagc 360
tttaaaaagc agcagaagca agcacttcta gccagaccct caagcaccat cacttaccta 420
actgacagcc caaagccagc attatgtgta actctggcag gactaatccc ctctgttTgt 480
ccaccactgg tcatgtgat gacaaaaact tatattccca tattagcttt tactcagatg 540
gcttatggag ccagtttctt atctttcttg ggtgggatca gatgggggtt tgctctacca 600
gaaggtagtc cagccaaacc agactacctt aatttagcta gcagtgcagc tctcttttcc 660
ttttcatggg ttgccttctt tatttctgaa agacttagtg aagccatagt cacagtaata 720
atgggtatgg gagtagcatt ccaccttgaa ctttttctct taccacatta tcccaactgg 780
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gtagttaaaa gtagtTttcc agaaaaagga cataagagac ctggtcaagt ataaaaaata 900
taaaagtctg ggaagtggag agcacctctg cccagctgct gcccgcTctg ggaagtgagg 960
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tcatagtata ttagttttca ctcagtcatt ttatgaataa tatagttatc cacttaaaca 1380
tttcaatatt ttaaccatct tgaaaattaa agattaaaaa tccccttaaa aaaaaaaaaa 1440
aa

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1442

&lt;210&gt; 48

&lt;211&gt; 247

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 48

Met Leu Arg Phe Ile Gln Lys Phe Ser Gln Ala Ser Ser Lys Ile Leu  
 1 5 10 15

Lys Tyr Ser Phe Pro Val Gly Leu Arg Thr Ser Arg Thr Asp Ile Leu  
 20 25 30

Ser Leu Lys Met Ser Leu Gln Gln Asn Phe Ser Pro Cys Pro Arg Pro  
 35 40 45

Trp Leu Ser Ser Ser Phe Pro Ala Tyr Met Ser Lys Thr Gln Cys Tyr  
 50 55 60

His Thr Ser Pro Cys Ser Phe Lys Lys Gln Gln Lys Gln Ala Leu Leu  
 65 70 75 80

Ala Arg Pro Ser Ser Thr Ile Thr Tyr Leu Thr Asp Ser Pro Lys Pro  
 85 90 95

Ala Leu Cys Val Thr Leu Ala Gly Leu Ile Pro Phe Val Ala Pro Pro  
 100 105 110

Leu Val Met Leu Met Thr Lys Thr Tyr Ile Pro Ile Leu Ala Phe Thr  
 115 120 125

Gln Met Ala Tyr Gly Ala Ser Phe Leu Ser Phe Leu Gly Gly Ile Arg  
 130 135 140

Trp Gly Phe Ala Leu Pro Glu Gly Ser Pro Ala Lys Pro Asp Tyr Leu  
 145 150 155 160

Asn Leu Ala Ser Ser Ala Ala Pro Leu Phe Phe Ser Trp Phe Ala Phe  
 165 170 175

Leu Ile Ser Glu Arg Leu Ser Glu Ala Ile Val Thr Val Ile Met Gly  
 180 185 190

Met Gly Val Ala Phe His Leu Glu Leu Phe Leu Leu Pro His Tyr Pro  
 195 200 205

Asn Trp Phe Lys Ala Leu Arg Ile Val Val Thr Leu Leu Ala Thr Phe  
 210 215 220

Ser Phe Ile Ile Thr Leu Val Val Lys Ser Ser Phe Pro Glu Lys Gly  
 225 230 235 240

His Lys Arg Pro Gly Gln Val  
 245

&lt;210&gt; 49

&lt;211&gt; 2696

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 49

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 aggttgatg ggggggcagg gacagtgtg ctgggaagga tgccagctct gggattgggc 120  
 cagtcctgtg ggcaagactt gcaagaggct ggatcaactt ggtgtggtat ctctgatggc 180  
 ttagagtaat ggcaatgagg gtctctgttg tgatgtcact gagtactttc tgggggtgctt 240  
 ctgggcaccc cttatgatgt cacaggaagc agttcctcag aggttacttc ctgtgaacat 300

35,

```

aagggagcag gtacttcctg tgatgtctca atgagttctt ccttgaaggt cactttggtg 360
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gctgaagcat gtacttcctg tattggacag tgaccagtct ctgacctgcc ttctccctcc 480
acacccttct ttggtgggtg ttggcctggg ggtcttccca ggaagagaat aaggcacggg 540
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attcaaacac gtcaagtctg cgaactcgcc ctggaggagg ggggtgggaga tggacctagt 660
gcaaaactact gttaaagacc tcccttccca cccctgcctt ttgtgtgcat gcctgtgtct 720
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caagtgtctt cctccctttc tttgtctggc tccctatgac tttctatttt ttttccctcc 2580
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tcctcaaatg tctcaactct ctctccccaa tttcccccatt taaaaaaaa aaaaaa 2696

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&lt;210&gt; 50

&lt;211&gt; 73

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 50

```

Met Asn Ser Phe Ala Tyr His Ser His Pro Pro Leu Gly Ser Arg Phe
  1                      5                      10                      15

```

```

Leu Gln Thr His Ser Leu Glu Ser Gly Ser Gln Ser Ala Gly Ser Arg
  20                      25                      30

```

```

Thr Pro Leu Thr Gln Thr His Leu Arg Arg Leu Gly Leu Leu Lys Ser
  35                      40                      45

```

```

Val Cys Leu Gly Cys Leu Cys Asn Asn Pro Ser Leu Phe Ile Phe Leu
  50                      55                      60

```

```

Gly Asp Pro Leu Pro Ser Gln Pro Gly
  65                      70

```

<210> 51  
<211> 2791  
<212> DNA  
<213> Homo sapiens

<400> 51

```
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caacctccgc ctcccggttt caagagattc tcctgcctca gcctcctaag tagctgggat 240
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catggttggtc aggtctggtc tgaactcccg acctcagggtg atccgcccac ctcggttcc 360
caaagtgtcg ggattacaag cgtgagccac tgcgcccagc cagtaactgc catttctaaa 420
gaggaaagag agcaggcaga gggtcctgac tcccagggga caggtagttc agctggacaa 480
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aaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 2791
```

<210> 52  
<211> 219  
<212> PRT  
<213> Homo sapiens

<400> 52

Met Ser Pro Gly Trp Ile Arg Leu Pro Thr Ser Ser Gln Thr Glu Ile  
 1 5 10 15

Leu Met Leu Pro Val Leu Ser Ala Thr Leu Gln Val Arg Thr Ser Cys  
 20 25 30

Pro Ser Phe Val Leu Val Thr Arg Pro Val Ser Ser Thr Met Lys Ile  
 35 40 45

Arg Phe Arg Phe Leu Ser Pro Gly Leu Ile Ser Phe Thr Lys Val Ser  
 50 55 60

Val Val Met Leu Pro Glu Pro Arg His Pro Thr Gly Trp Gly Ile Glu  
 65 70 75 80

Asp Glu Gly Ser Met Leu Gly Ser Phe Ala Pro Met Leu His Phe Pro  
 85 90 95

Arg Pro Thr Tyr Pro Ile Arg Met Gly Ser Gly Ser Leu Asn Pro Ser  
 100 105 110

Asn Pro Ser Lys Arg Leu Lys Lys Asn Ile Pro Gly Gly Leu Gln Leu  
 115 120 125

Gln Asp Gln Asn Leu Gly Val Ser Gly Gln Ala Ala Leu Gly Leu Glu  
 130 135 140

Gly Pro Leu Pro Gly Cys Ser Phe Ser Leu Lys Pro Arg Ser Gly Gly  
 145 150 155 160

Ala Asp Val Asp Arg Gly Arg Glu Pro Gly Ala Gln Pro Gly Ser Arg  
 165 170 175

Ile Leu Leu Ala Arg Ser Ser Gly Thr Leu Ile Pro Thr Ser Arg Asp  
 180 185 190

Ser Val His Pro Leu Pro Tyr Arg Gln Pro Thr Thr His Pro Ser Gln  
 195 200 205

Pro Ala Gly Leu Cys Arg Gly Trp Lys Leu Leu  
 210 215

&lt;210&gt; 53

&lt;211&gt; 1527

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 53

tgaacaacaa gctaaaatgg aatagcacag aatggctgag gagccactgt gaagaaaggc 60  
 atgcagccat gaaactgcag tgtcccttgc tgtagtgagg gtggctctga ccaatctgga 120  
 agatacagaa aatgccaaga gagcctacgc agaagcagtc cacctggata agtgtaaccc 180  
 tttagtaaac ctgaactatg ctgtgctgct gtacaaccag ggcgagaaga agaacgccct 240  
 ggcccaatat caggagatgg agaagaaagt cagcctactc aaggacaata gctctctgga 300  
 atttgactct gagatgggtg agatggctca gaagttggga gctgctctcc aggttgggga 360  
 ggactggtc tggaccaaac cagttaaaga tcccaaatca aagcaccaga ccacttcaac 420  
 cagcaaacct gccagtttcc agcagcctct gggctctaata caagctctag gacaggcaat 480  
 gtcttcagca gctgcataca ggacgctccc ctacgggtgct ggaggaacat ccagttcac 540  
 aaagccccca tctcttcttc tggagccaga gcctgcggtg gaatcaagtc caactgaaac 600  
 atcagaacaa ataagagaga aataagaata gaatgaatga ccccaaaata gggttttctt 660  
 gggcgaggat gtgctggatt aggaaagggtg acatgacaca ggcagagcag agtggcacc 720



```

accacagaat acagtgtgtg ttattacgag gagccagcag ttgagcctaa ggtccttcta 780
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tgaaaagaga acacagttcc tttaagaact ggcagcaagg cttgaggcct tatgtatgta 900
gctgagtcag caaggtacat gatgctgtct gctttcaaaa ggacttttct ctctagctg 960
actgactcct tccttagttc aaggaacagc tgagacagac ctctgctgag tagctctgtg 1020
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taaaagaacc taaaaaaaaa aaaaaaa 1527

```

&lt;210&gt; 54

&lt;211&gt; 122

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 54

```

Met Glu Lys Lys Val Ser Leu Leu Lys Asp Asn Ser Ser Leu Glu Phe
  1                      5                      10                      15

```

```

Asp Ser Glu Met Val Glu Met Ala Gln Lys Leu Gly Ala Ala Leu Gln
      20                      25                      30

```

```

Val Gly Glu Ala Leu Val Trp Thr Lys Pro Val Lys Asp Pro Lys Ser
    35                      40                      45

```

```

Lys His Gln Thr Thr Ser Thr Ser Lys Pro Ala Ser Phe Gln Gln Pro
    50                      55                      60

```

```

Leu Gly Ser Asn Gln Ala Leu Gly Gln Ala Met Ser Ser Ala Ala Ala
    65                      70                      75                      80

```

```

Tyr Arg Thr Leu Pro Ser Gly Ala Gly Gly Thr Ser Gln Phe Thr Lys
      85                      90                      95

```

```

Pro Pro Ser Leu Pro Leu Glu Pro Glu Pro Ala Val Glu Ser Ser Pro
    100                      105                      110

```

```

Thr Glu Thr Ser Glu Gln Ile Arg Glu Lys
    115                      120

```

&lt;210&gt; 55

&lt;211&gt; 2352

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 55

```

agcagagtga gctgaagctc ctgaggaggg ttcccgaagg ggggcgctca gagatggggg 60
cagggggcgg ggagaggaga gtctgcctta tgtcccttcc ttgtggactt cacatgggtca 120
tgcaggaaagt gaggatgggt gtccagcggg ggccgaggcc actagtatcc tcctgcttcc 180
cctgccatt ctccagggct ggactgaccc tatggactgg gagagagtgc ctgaggccac 240
catgccacag tcaaaggggg tcctatctca gaaggtggca gcatccactg agatatcctc 300
acccgaaggg aaggaggctg ctgggtagca aataagcccc ttcttttctt ggtgagttga 360
tgacctccaa tagctcccag tgtcatgggt acccagtagc cattagctgg tgttgggttg 420
attgagacct ggggcagttc ctggggcagg aagccagatg ggagatgaga tagaaagtgt 480
taggagttat cctctttgcc tggcctttga gaataactta ctgtgtgact ttgggcaagt 540
tccttcccca ctctgggctt cagtttctca cttgggaaag caaggagttt gaccagatga 600

```

```

tcacaatggg ccttcctagc tctggccacc aagaatttgt gaacattaga gctcctgggc 660
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ctcagaggtg gcagggccct atggagcacc aactgccctc aaocccaccc tgtgcccaag 780
actgggaagg gattgatgtc aggctgtggc cataggtagc atgagttgcc caaggagggg 840
cagagcatat ctttgctgag gcttggctga ggggcttatg atagggcttg cagtacctca 900
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aaaaaaaaaa aa                                     2352

```

&lt;210&gt; 56

&lt;211&gt; 169

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 56

```

Met Lys Cys Trp Ser Asn Ala Trp Gln Thr Tyr Ala Leu Gln Cys Leu
  1             5             10             15

```

```

Leu Lys Pro Leu Gly Leu Thr Gln Asp Pro Leu Val Phe Gly Met Thr
      20             25             30

```

```

Ser Phe Leu Gln Thr Ser Ser Pro Ile Pro Asn Ser Cys Met Glu Asn
      35             40             45

```

```

Val Cys Gln Ala Gly Phe Pro Ser Leu Leu His Leu Asn Ile Thr Leu
      50             55             60

```

```

Thr Leu Leu Gly Leu Ala Gln Cys Tyr Leu Ala Asn Phe Ser Ser Cys
      65             70             75             80

```

```

Arg Glu Gly Ser Glu His Tyr Leu Phe Phe Phe Phe Ser Trp Ser
      85             90             95

```

```

Gln Asp Cys Thr Arg Gln Trp Pro Asn Leu Val Glu Phe Ser Leu Pro
      100            105            110

```

```

Ser Phe Ala Asp Asp Ser Ala Leu Cys Gln Val Leu Glu Pro Gln Arg
      115            120            125

```

40

Trp Val Ser Pro Ser Pro Cys Pro Gln Glu Ala His Gly Gln Gly Asn  
 130 135 140

Val Val Gly Ile Ser Asn Arg Gly Gln Leu Pro Ser Gly Leu Leu Val  
 145 150 155 160

Ala Ala Gly Pro Tyr Gly Ala Leu Met  
 165

<210> 57  
 <211> 995  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> (852)

<400> 57  
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 gtgagccaag atcgaccac tgcactccag cctgggtgac agagcgagac tctgtctcaa 180  
 aaaaaaaaaa aaaaaagaaa agaaaaaaaaac ctattgccta cctcccaagg gcaaattgcag 240  
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 gtatacgagg ggtttttttt tgtttgtttt gccwagaatg atcctccctg gtgaatctta 420  
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 gtaattttta catgatcttt ctgggccaaa attttcttat ctgtaaaatg aagatgttg 720  
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 tctacctgta aaggaatgaa gttggacccc ttctcatac tatacacaaa aattaactca 840  
 aaatggatca tngacctaaa cataagagct aaaactataa gactttcaga agaaaacaca 900  
 ggagtaagtc ttcattgacct tggattaagg aatggttgc tagatatgac acccaaaaaa 960  
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaa 995

<210> 58  
 <211> 72  
 <212> PRT  
 <213> Homo sapiens

<400> 58  
 Met Leu Tyr Cys Leu Pro Leu Ser Leu Asp Leu Glu Ile Leu Lys Asn  
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Arg Asn Lys Lys Phe Ser Leu Ser Leu Tyr Val Leu Phe Leu Leu Leu  
 20 25 30

Leu Leu Leu Thr Trp Tyr Ile Phe Phe Gln Met Tyr Phe Leu Leu Phe  
 35 40 45

Ser Thr Gln Ser Asn Phe Asn Met Ile Phe Leu Gly Gln Asn Phe Leu  
 50 55 60

Ile Cys Lys Met Lys Met Leu Asp  
 65 70

<210> 59  
 <211> 1038

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 59

```

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gatgaggcgc tgggctggct ctccacctcc acttccgaag ctgcccagat agcctgagtg 180
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ccactcaagt cagagaaaca tgaggaataa aggtcacatg cagatgcata aaaaaaaaaa 1020
aaaaaaaaaa aaaaaaaaaa                                     1038

```

&lt;210&gt; 60

&lt;211&gt; 105

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; UNSURE

&lt;222&gt; (61)

&lt;220&gt;

&lt;221&gt; UNSURE

&lt;222&gt; (65)

&lt;400&gt; 60

```

Met Gly Phe Thr Gly Ala Gly Ile Ala Ala Ser Ser Ile Ala Ala Lys
 1               5               10               15

Met Met Ser Ala Ala Ala Ile Ala Asn Gly Gly Gly Val Ser Ala Gly
 20               25               30

Ser Leu Val Ala Thr Leu Gln Ser Val Gly Ala Ala Gly Leu Ser Thr
 35               40               45

Ser Ser Asn Ile Leu Leu Ala Ser Val Gly Ser Val Xaa Gly Ala Cys
 50               55               60

Xaa Gly Asn Ser Pro Ser Ser Ser Leu Pro Ala Glu Pro Glu Ala Lys
 65               70               75               80

Glu Asp Glu Ala Arg Glu Asn Val Pro Gln Gly Glu Pro Pro Lys Pro
 85               90               95

Pro Leu Lys Ser Glu Lys His Glu Glu
 100               105

```

&lt;210&gt; 61

&lt;211&gt; 1060

&lt;212&gt; DNA

<213> Homo sapiens

<400> 61

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gaggcctgcc cgtgccccctg gaccagaccc tgccttgaa tgtgaatcca gccctgccct 180
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```

<210> 62

<211> 256

<212> PRT

<213> Homo sapiens

<400> 62

```

Met Phe Gln Thr Gly Gly Leu Ile Val Phe Tyr Gly Leu Leu Ala Gln
  1             5             10             15

Thr Met Ala Gln Phe Gly Gly Leu Pro Val Pro Leu Asp Gln Thr Leu
      20             25             30

Pro Leu Asn Val Asn Pro Ala Leu Pro Leu Ser Pro Thr Gly Leu Ala
      35             40             45

Gly Ser Leu Thr Asn Ala Leu Ser Asn Gly Leu Leu Ser Gly Gly Leu
      50             55             60

Leu Gly Ile Leu Glu Asn Leu Pro Leu Leu Asp Ile Leu Lys Pro Gly
      65             70             75             80

Gly Gly Thr Ser Gly Gly Leu Leu Gly Gly Leu Leu Gly Lys Val Thr
      85             90             95

Ser Val Ile Pro Gly Leu Asn Asn Ile Ile Asp Ile Lys Val Thr Asp
      100            105            110

Pro Gln Leu Leu Glu Leu Gly Leu Val Gln Ser Pro Asp Gly His Arg
      115            120            125

Leu Tyr Val Thr Ile Pro Leu Gly Ile Lys Leu Gln Val Asn Thr Pro
      130            135            140

Leu Val Gly Ala Ser Leu Leu Arg Leu Ala Val Lys Leu Asp Ile Thr
      145            150            155            160

Ala Glu Ile Leu Ala Val Arg Asp Lys Gln Glu Arg Ile His Leu Val
      165            170            175

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Leu Gly Asp Cys Thr His Ser Pro Gly Ser Leu Gln Ile Ser Leu Leu  
 180 185 190

Asp Gly Leu Gly Pro Leu Pro Ile Gln Gly Leu Leu Asp Ser Leu Thr  
 195 200 205

Gly Ile Leu Asn Lys Val Leu Pro Glu Leu Val Gln Gly Asn Val Cys  
 210 215 220

Pro Leu Val Asn Glu Val Leu Arg Gly Leu Asp Ile Thr Leu Val His  
 225 230 235 240

Asp Ile Val Asn Met Leu Ile His Gly Leu Gln Phe Val Ile Lys Val  
 245 250 255

<210> 63  
 <211> 992  
 <212> DNA  
 <213> Homo sapiens

<400> 63  
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 ttctcaacct tgacaccatt gacatttttg actgggtaat tctttgttct gcagagctgt 180  
 cttttgcaat gtaggagatt tactaatatc cctggcctct acccagtagt accactagca 240  
 cctattcccc acccagcgtg tctccagata ttgtcaaata tcccatcggg tgcaaaatga 300  
 tccctgggtca agatctgttg cccaagatgt tacaggtaac aatgaccaca ttgaaattg 360  
 ttttcccttt cattttaccc tgtgaaagca tctctcctag agccttgcaa gaggcagggtg 420  
 acattgtgtc catatttctt cctgtttcag aacttctgtt tcacaacaat ttctctctcg 480  
 ctacaagtat tctttcactc agcactgggg aagttgggaa cagctgggtca ccatcatccc 540  
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 gattggtacc agaagagggc taagatacgt tttctgtctt gagctgaaag cacagtctac 840  
 tctccttcgt tttgtcgatg agaaagttga ggccagaggg gaggtgacat gtttagagtc 900  
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<210> 64  
 <211> 82  
 <212> PRT  
 <213> Homo sapiens

<400> 64  
 Met Ile Pro Gly Gln Asp Leu Leu Pro Lys Met Leu Gln Val Thr Met  
 1 5 10 15  
 Thr Thr Phe Glu Ile Val Phe Pro Phe Ile Leu Pro Cys Glu Ser Ile  
 20 25 30  
 Ser Pro Arg Ala Leu Gln Glu Ala Gly Asp Ile Val Ser Ile Phe Leu  
 35 40 45  
 Pro Val Ser Glu Leu Leu Phe His Asn Asn Phe Ser Leu Ala Thr Ser  
 50 55 60  
 Ile Leu Ser Leu Ser Thr Gly Glu Val Gly Asn Ser Trp Ser Pro Ser  
 65 70 75 80  
 Ser Leu

44

<210> 65  
 <211> 1095  
 <212> DNA  
 <213> Homo sapiens

<400> 65  
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 ctgatcatcc cattgtactg caaaaaccag aaaacaacca aagttttaag tagcatttta 180  
 agaacagatg aatttaagtt tggacatctg caaatgaggt ggatctagca acaataactg 240  
 taatggactg tgacaattca atttattctt aattttgatg gttggctatt tgacttctct 300  
 aaaaatgaga aagagctatt ttaaaatata aagaattttc taatcagttt cagctttgca 360  
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 gggaagactg tatatttata atttgcatac tacttgcaat tttttgtttt tcatcacttg 480  
 taataatgga atggaaatgt aagctgtaaa gactctcaaa tataaaatat ttgctacagt 540  
 gtatatatgg tacataattg cttgttgctt ttaaagttcc ttctgttggt ctgcttccca 600  
 ctgatttcat accagctcat gaatggatca ttacagtctc tccagaggct tagaatgatt 660  
 cagaatgttc aatgcattga tctcaataaa caggaggcag aatttttaat gggattttct 720  
 tttcagatat atgattgggtc tctaggtttt tgataataat atggtcttaa attcataatt 780  
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 aaaactgata tttttatttc caaaggaatt tagacatttg aaaataattg acatacatta 960  
 agttttaatt cgataatttc ttatatatgg atgaacaatt tttgggttta agcttttaat 1020  
 tcttagaaat tttatacatt aaatctctct caatttgtca ctctggatgt tactgtttta 1080  
 aaaaaaaaaa aaaaa 1095

<210> 66  
 <211> 68  
 <212> PRT  
 <213> Homo sapiens

<400> 66  
 Met Val His Asn Cys Leu Leu Leu Lys Phe Leu Leu Leu Phe Cys  
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 Phe Pro Leu Ile Ser Tyr Gln Leu Met Asn Gly Ser Leu Gln Ser Leu  
 20 25 30  
 Gln Arg Leu Arg Met Ile Gln Asn Val Gln Cys Ile Val Leu Asn Lys  
 35 40 45  
 Gln Glu Ala Glu Phe Leu Met Gly Ile Ser Phe Gln Ile Tyr Asp Trp  
 50 55 60  
 Ser Leu Gly Phe  
 65

<210> 67  
 <211> 831  
 <212> DNA  
 <213> Homo sapiens

<400> 67  
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 cctgggaaag aggggctgag gcctgaactg ggcctaagga gaggcagct cagttcgcac 180  
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 cagagctctg cagccccaag tggcagctgc tggctcaaag ctgggactac atgaaagtct 300  
 gaaaagagaa tgagaaggag gtggcgcaag agcctggacg cacgtgtggg aggccgtttt 360  
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45

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cccarcgtgc ggggggtgtgc tkgtggccct gtgggcctgt agggcaaccc atgccaactg 480
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gttggtcattg ttattaggaa gcaaaaaaat gtacagttac aagaatcatt ttccaaacag 600
agggttaaata tgagctgaaa agtgtaaaaa aggaagagga acatcacttt acaaatcatt 660
aaattaaaca aataaacaaa cagaacccaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 720
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 780
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa a          831

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<210> 68  
 <211> 50  
 <212> PRT  
 <213> Homo sapiens

<220>  
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 <222> (29)

<220>  
 <221> UNSURE  
 <222> (39)

<220>  
 <221> UNSURE  
 <222> (45)

<400> 68  
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   1                  5                  10                  15  
 Phe Val Gln Arg Tyr Cys Ala Pro Arg Ala Gly Met Xaa Ser Arg Ser  
           20                  25                  30  
 Val Ala Leu Leu Val Pro Xaa Val Arg Gly Cys Ala Xaa Gly Pro Val  
       35                  40                  45  
 Gly Leu  
   50

<210> 69  
 <211> 1893  
 <212> DNA  
 <213> Homo sapiens

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ttacctccca ratactattt tttggatttg ggtggctttt cttcatgcgc caattgttta 180
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tttttctcta tctactgtgt ttggaaaatt ttcatgaata ccatcaatat tgtatttgat 1020

```



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cgagttggga aaacggatcc tgtcacaaga ggcattgaga tcaactgtgaa ttatctggga 1080
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atcgtcacat ccatcagagg attgctgac actcttaacca agttctttta tgccatctct 1200
agcagtaagt cctccaatgt cattgtcctg ctatttagcac agataatggg catgtacttt 1260
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aaaatcagag actgtaacaa aaaaaaaaaa aaa 1893

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&lt;210&gt; 70

&lt;211&gt; 309

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 70

```

Met Ser Phe Leu Ile Asp Ser Ser Ile Met Ile Thr Ser Gln Ile Leu
  1                      5                      10                      15

```

```

Phe Phe Gly Phe Gly Trp Leu Phe Phe Met Arg Gln Leu Phe Lys Asp
      20                      25                      30

```

```

Tyr Glu Ile Arg Gln Tyr Val Val Gln Val Ile Phe Ser Val Thr Phe
  35                      40                      45

```

```

Ala Phe Ser Cys Thr Met Phe Glu Leu Ile Ile Phe Glu Ile Leu Gly
  50                      55                      60

```

```

Val Leu Asn Ser Ser Ser Arg Tyr Phe His Trp Lys Met Asn Leu Cys
  65                      70                      75                      80

```

```

Val Ile Leu Leu Ile Leu Val Phe Met Val Pro Phe Tyr Ile Gly Tyr
      85                      90                      95

```

```

Phe Ile Val Ser Asn Ile Arg Leu Leu His Lys Gln Arg Leu Leu Phe
  100                      105                      110

```

```

Ser Cys Leu Leu Trp Leu Thr Phe Met Tyr Phe Phe Trp Lys Leu Gly
  115                      120                      125

```

```

Asp Pro Phe Pro Ile Leu Ser Pro Lys His Gly Ile Leu Ser Ile Glu
  130                      135                      140

```

```

Gln Leu Ile Ser Arg Val Gly Val Ile Gly Val Thr Leu Met Ala Leu
  145                      150                      155                      160

```

```

Leu Ser Gly Phe Gly Ala Val Asn Cys Pro Tyr Thr Tyr Met Ser Tyr
  165                      170                      175

```

```

Phe Leu Arg Asn Val Thr Asp Thr Asp Ile Leu Ala Leu Glu Arg Arg
  180                      185                      190

```

```

Leu Leu Gln Thr Met Asp Met Ile Ile Ser Lys Lys Lys Arg Met Ala
  195                      200                      205

```

47

Met Ala Arg Arg Thr Met Phe Gln Lys Gly Glu Val His Asn Lys Pro  
 210 215 220

Ser Gly Phe Trp Gly Met Ile Lys Ser Val Thr Thr Ser Ala Ser Gly  
 225 230 235 240

Ser Glu Asn Leu Thr Leu Ile Gln Gln Glu Val Asp Ala Leu Glu Glu  
 245 250 255

Leu Ser Arg Gln Leu Phe Leu Glu Thr Ala Asp Leu Tyr Ala Thr Lys  
 260 265 270

Glu Arg Ile Glu Tyr Ser Lys Thr Phe Lys Gly Lys Tyr Leu Ile Ser  
 275 280 285

Trp Leu Leu Phe Leu Tyr Leu Leu Cys Leu Glu Asn Phe His Glu Tyr  
 290 295 300

His Gln Tyr Cys Ile  
 305

<210> 71  
 <211> 1424  
 <212> DNA  
 <213> Homo sapiens

<400> 71  
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 tctacttaat attctcgtgc tcagagctaa cgaggctggc gttaggcggg gacgtggggcc 180  
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 gtttccagct gacagctgct acctgcaggt gctgctcgag tctgtctctg gttcaccata 360  
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 ctccccactt tccccaaacc tgcagtcagc accccagggc tctggaggct gtacaggat 780  
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 cagtgaagca aaaccatgcc actgcactcc agcctgggca acagagtga acgcgggtctc 1260  
 aaaaaaagaa gaaagaaaga aagaaagaaa gaaagaaaga aataaagaaa gagagagaga 1320  
 gagagagaga gagagagaga aagaaagaaa aagaaagaaa gaaagaaaga 1380  
 aagaaagaaa gaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaa 1424

<210> 72  
 <211> 70  
 <212> PRT  
 <213> Homo sapiens

<400> 72  
 Met Thr Ser Glu His Ala Thr Leu Arg Ser Leu Ser Ala Leu Pro Thr  
 1 5 10 15

48.

Phe Pro Asn Pro Ala Val Ser Thr Pro Gly Leu Trp Arg Leu Tyr Arg  
 20 25 30  
 Tyr Glu Met Gln Arg Ala Cys Gly Leu Gly Val Ser Val Val Trp Gly  
 35 40 45  
 Cys Gly Gly Ser Pro Val Trp His Gly Cys Glu Gly Ala Val Glu Asp  
 50 55 60  
 Arg Leu Ser Val Leu Pro  
 65 70

<210> 73  
 <211> 1726  
 <212> DNA  
 <213> Homo sapiens

<400> 73  
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 taatgataat aaaggaattg tatctaggaa aaaaaaaaaa aaaaaa 1726

<210> 74  
 <211> 133  
 <212> PRT  
 <213> Homo sapiens

<400> 74  
 Met Val Ser Ser Trp Pro Ala Arg Lys Ala Ser Leu Leu Cys Val Cys  
 1 5 10 15  
 Ala Val Leu Val Leu Pro Trp Arg Thr Leu Gly Ser Pro Val Ile Leu  
 20 25 30

49.

Ala Arg Arg Pro Gly Ala Trp Val Pro Ser Trp Lys Gly Thr Ser Tyr  
 35 40 45

Thr Pro Gln Pro His Phe Pro Thr Asn Phe Tyr Met Pro Trp Glu Asn  
 50 55 60

Leu Leu His Val Gly Cys Pro Leu Pro Leu Phe Gln Gln Cys Pro Val  
 65 70 75 80

Leu Leu Ile Asn Leu Arg Pro Ala Pro His Thr Leu Pro Cys Ala Ser  
 85 90 95

Ala Ser Arg Tyr Ser Arg Gln Pro Asn Val Val Glu Ala Arg Trp Ile  
 100 105 110

Pro Gly Ser Ser Trp Pro Met Asp Val Ser His His Ser Ile Leu Glu  
 115 120 125

Thr Glu Lys Arg Ser  
 130

<210> 75  
 <211> 927  
 <212> DNA  
 <213> Homo sapiens

<400> 75  
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 ttcttcaaat ccaaaaaaaa aaaaaaa 927

<210> 76  
 <211> 142  
 <212> PRT  
 <213> Homo sapiens

<400> 76  
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 1 5 10 15

Pro Arg Ser Gln Pro Ile Asn Leu Asn His Tyr Ala Thr Lys Lys Ser  
 20 25 30

Val Ala Glu Ser Met Leu Asp Val Ala Leu Phe Met Ser Asn Ala Met  
 35 40 45

Arg Leu Lys Ala Val Leu Glu Gln Gly Pro Ser Ser His Tyr Tyr Thr  
 50 55 60

50.

Thr Leu Val Thr Leu Ile Ser Leu Ser Leu Leu Leu Gln Val Val Ile  
65 70 75 80

Gly Val Leu Leu Val Val Ile Ala Arg Leu Asn Leu Asn Glu Val Glu  
85 90 95

Lys Gln Trp Arg Leu Asn Gln Leu Asn Asn Ala Ala Thr Ile Leu Val  
100 105 110

Phe Phe Thr Val Val Ile Asn Val Phe Ile Thr Ala Phe Gly Ala His  
115 120 125

Lys Thr Gly Phe Leu Ala Ala Arg Ala Ser Arg Asn Pro Leu  
130 135 140

&lt;210&gt; 77

&lt;211&gt; 1660

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 77

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&lt;210&gt; 78

&lt;211&gt; 447

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 78

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51,

Ile Leu Cys Leu Leu Glu Met Ser Phe Ala Val Pro Phe Phe Pro Gln  
20 25 30

Gln Ser Gly Thr Pro Gly Met Ala Ser Leu Ser Leu Glu Thr Met Arg  
35 40 45

Gln Leu Gly Ser Leu Gln Arg Leu Asn Thr Leu Ser Gln Tyr Ser Arg  
50 55 60

Tyr Gly Phe Gly Lys Ser Phe Asn Ser Leu Trp Met His Gly Leu Leu  
65 70 75 80

Pro Pro His Ser Ser Leu Pro Trp Met Arg Pro Arg Glu His Glu Thr  
85 90 95

Gln Gln Tyr Glu Tyr Ser Leu Pro Val His Pro Pro Pro Leu Pro Ser  
100 105 110

Gln Pro Ser Leu Lys Pro Gln Gln Pro Gly Leu Lys Pro Phe Leu Gln  
115 120 125

Ser Ala Ala Ala Thr Thr Asn Gln Ala Thr Ala Leu Lys Glu Ala Leu  
130 135 140

Gln Pro Pro Ile His Leu Gly His Leu Pro Leu Gln Glu Gly Glu Leu  
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Pro Leu Val Gln Gln Gln Val Ala Pro Ser Asp Lys Pro Pro Lys Pro  
165 170 175

Glu Leu Pro Gly Val Asp Phe Ala Asp Pro Gln Gly Pro Ser Leu Pro  
180 185 190

Gly Met Asp Phe Pro Asp Pro Gln Gly Pro Ser Leu Pro Gly Leu Asp  
195 200 205

Phe Ala Asp Pro Gln Gly Ser Thr Ile Phe Gln Ile Ala Arg Leu Ile  
210 215 220

Ser His Gly Pro Met Pro Gln Asn Lys Gln Ser Pro Leu Tyr Pro Gly  
225 230 235 240

Met Leu Tyr Val Pro Phe Gly Ala Asn Gln Leu Asn Ala Pro Ala Arg  
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Leu Gly Ile Met Ser Ser Glu Glu Val Ala Gly Gly Arg Glu Asp Pro  
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Met Ala Tyr Gly Ala Met Phe Pro Gly Phe Gly Gly Met Arg Pro Gly  
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Phe Glu Gly Met Pro His Asn Pro Ala Met Gly Gly Asp Phe Thr Leu  
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Glu Phe Asp Ser Pro Val Ala Ala Thr Lys Gly Pro Glu Asn Glu Glu  
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340 345 350

Leu Leu Ala Leu Pro Lys Asp Asp Ile Pro Gly Leu Pro Arg Ser Pro  
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Ser Gly Lys Met Lys Gly Leu Pro Ser Val Thr Pro Ala Ala Ala Asp  
 370 375 380

Pro Leu Met Thr Pro Glu Leu Ala Asp Val Tyr Arg Thr Tyr Asp Ala  
 385 390 395 400

Asp Met Thr Thr Ser Val Asp Phe Gln Glu Glu Ala Thr Met Asp Thr  
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<210> 79

<211> 2036

<212> DNA

<213> Homo sapiens

<400> 79

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<210> 80

53.

<211> 81  
 <212> PRT  
 <213> Homo sapiens

<400> 80  
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                   20                          25                          30  
 Leu Leu His Pro Thr Val Ala Ser Val Val Trp Thr Trp Trp Leu Leu  
           35                          40                          45  
 His Pro Thr Gln Gly Asn Ser Val Leu Leu His Pro Thr Asp Cys Trp  
           50                          55                          60  
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<210> 81  
 <211> 3465  
 <212> DNA  
 <213> Homo sapiens

<400> 81  
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&lt;210&gt; 82

&lt;211&gt; 51

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 82

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  1           5           10           15

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Met Trp Ile Tyr Ala Thr Asp Leu His Phe Gly His His Lys Lys Tyr
      20           25           30

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Cys Cys Ala Ser Pro Thr Pro Thr Pro Thr Pro Leu Val Tyr Ser Leu
      35           40           45

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Lys Trp Tyr
      50

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&lt;210&gt; 83

&lt;211&gt; 808

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 83

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55

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 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 808

<210> 84  
 <211> 45  
 <212> PRT  
 <213> Homo sapiens

<400> 84  
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<210> 85  
 <211> 1024  
 <212> DNA  
 <213> Homo sapiens

<400> 85  
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<210> 86  
 <211> 64  
 <212> PRT  
 <213> Homo sapiens

<400> 86  
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 Ser Leu Cys His Pro Gln Ala Ser Leu Gly Val Lys Arg Lys Leu Ser  
 35 40 45

56

Thr Asp Thr Ala Met Arg Ser His Val Leu Met Pro Ser Gly Ala Gln  
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<210> 87  
 <211> 867  
 <212> DNA  
 <213> Homo sapiens

<400> 87  
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<210> 88  
 <211> 51  
 <212> PRT  
 <213> Homo sapiens

<400> 88  
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Phe Leu Ile Cys Ser Lys Glu Asn Ala Ala Ile Leu His Ser Leu Trp  
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Lys Glu Thr Lys Gln Asn Lys Thr His Ser Lys Pro Ala Val Leu Leu  
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Ser Asp Lys  
 50

<210> 89  
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 <212> DNA  
 <213> Homo sapiens

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&lt;210&gt; 90

&lt;211&gt; 245

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 90

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  1              5              10              15
Phe Lys Ser Val Leu Leu Ile Tyr Thr Phe Ile Phe Trp Ile Thr Gly
  20              25              30
Val Ile Leu Leu Ala Val Gly Ile Trp Gly Lys Val Ser Leu Glu Asn
  35              40              45
Tyr Phe Ser Leu Leu Asn Glu Lys Ala Thr Asn Val Pro Phe Val Leu
  50              55              60
Ile Ala Thr Gly Thr Val Ile Ile Leu Leu Gly Thr Phe Gly Cys Phe
  65              70              75              80
Ala Thr Cys Arg Ala Ser Ala Trp Met Leu Lys Leu Tyr Ala Met Phe
  85              90              95
Leu Thr Leu Val Phe Leu Val Glu Leu Val Ala Ala Ile Val Gly Phe
 100              105              110
Val Phe Arg His Glu Ile Lys Asn Ser Phe Lys Asn Asn Tyr Glu Lys
 115              120              125
Ala Leu Lys Gln Tyr Asn Ser Thr Gly Asp Tyr Arg Ser His Ala Val
 130              135              140
Asp Lys Ile Gln Asn Thr Leu His Cys Cys Gly Val Thr Asp Tyr Arg
 145              150              155              160
Asp Trp Thr Asp Thr Asn Tyr Tyr Ser Glu Lys Gly Phe Pro Lys Ser
 165              170              175
Cys Cys Lys Leu Glu Asp Cys Thr Pro Gln Arg Asp Ala Asp Lys Val
 180              185              190

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58

Asn Asn Glu Gly Cys Phe Ile Lys Val Met Thr Ile Ile Glu Ser Glu  
 195 200 205

Met Gly Val Val Ala Gly Ile Ser Phe Gly Val Ala Cys Phe Gln Leu  
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Ile Gly Ile Phe Leu Ala Tyr Cys Leu Ser Arg Ala Ile Thr Asn Asn  
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Gln Tyr Glu Ile Val  
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<210> 91  
 <211> 1992  
 <212> DNA  
 <213> Homo sapiens

<400> 91  
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 gtatttatatg gcacaagatt cgacgtcggg gacaagatcc gctacagctg tgtaactgga 720  
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 acacatgcta catttcaaca aagatcattt cctccttaat ttaactacaa atgttaatta 1920  
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 aaaaaaaaaa aa 1992

<210> 92  
 <211> 556  
 <212> PRT  
 <213> Homo sapiens

<400> 92  
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 Arg Gly Phe Lys Leu Phe Pro Gly Lys Asp Asn Ser Asn Lys Phe Ser  
           355                          360                          365  
 Ile Leu Asn Glu Gly Gly Ile Lys Thr Ala Ser Asn Leu Cys Pro Asp  
           370                          375                          380  
 Pro Gly Glu Pro Glu Asn Gly Lys Arg Ile Gly Ser Asp Phe Ser Leu  
           385                          390                          395                          400  
 Gly Ser Thr Val Gln Phe Ser Cys Asp Glu Asp Tyr Val Leu Gln Gly  
                           405                          410                          415  
 Ala Lys Ser Ile Thr Cys Gln Arg Ile Ala Glu Val Phe Ala Ala Trp  
           420                          425                          430  
 Ser Asp His Arg Pro Val Cys Lys Val Lys Thr Cys Gly Ser Asn Leu  
           435                          440                          445  
 Gln Gly Pro Ser Gly Thr Phe Thr Ser Pro Asn Phe Pro Phe Gln Tyr  
           450                          455                          460  
 Asp Ser Asn Ala Gln Cys Val Trp Val Ile Thr Ala Val Asn Thr Asn  
           465                          470                          475                          480  
 Lys Val Ile Gln Ile Asn Phe Glu Glu Phe Asp Leu Glu Ile Gly Tyr  
                           485                          490                          495  
 Asp Thr Leu Thr Ile Gly Asp Gly Gly Glu Val Gly Asp Pro Arg Thr  
           500                          505                          510  
 Val Leu Gln Val Leu Thr Gly Ser Phe Val Pro Asp Leu Ile Val Ser  
           515                          520                          525  
 Met Ser Ser Gln Met Trp Leu His Leu Gln Thr Asp Glu Ser Val Gly  
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 <211> 2085  
 <212> DNA  
 <213> Homo sapiens

<400> 93  
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 ccacagaata agagaactcc agatttgcct gaagaagagt atgtgaagga agaaatccag 780

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&lt;210&gt; 94

&lt;211&gt; 399

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 94

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Met Ala Glu Ala Met Asp Leu Gly Lys Asp Pro Asn Gly Pro Thr His
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Ser Ser Thr Leu Phe Val Arg Asp Asp Gly Ser Ser Met Ser Phe Tyr
      20              25              30

Val Arg Pro Ser Pro Ala Lys Arg Arg Leu Ser Thr Leu Ile Leu His
      35              40              45

Gly Gly Gly Thr Val Cys Arg Val Gln Glu Pro Gly Ala Val Leu Leu
      50              55              60

Ala Gln Pro Gly Glu Ala Leu Ala Glu Ala Ser Gly Asp Phe Ile Ser
      65              70              75              80

Thr Gln Tyr Ile Leu Asp Cys Val Glu Arg Asn Glu Arg Leu Glu Leu
      85              90              95

Glu Ala Tyr Arg Leu Gly Pro Ala Ser Ala Ala Asp Thr Gly Ser Glu
      100              105              110

Ala Lys Pro Gly Ala Leu Ala Glu Gly Ala Ala Glu Pro Glu Pro Gln
      115              120              125

Arg His Ala Gly Arg Ile Ala Phe Thr Asp Ala Asp Asp Val Ala Ile
      130              135              140

Leu Thr Tyr Val Lys Glu Asn Ala Arg Ser Pro Ser Ser Val Thr Gly
      145              150              155              160

Asn Ala Leu Trp Lys Ala Met Glu Lys Ser Ser Leu Thr Gln His Ser
      165              170              175

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Trp Gln Ser Leu Lys Asp Arg Tyr Leu Lys His Leu Arg Gly Gln Glu  
 180 185 190  
 His Lys Tyr Leu Leu Gly Asp Ala Pro Val Ser Pro Ser Ser Gln Lys  
 195 200 205  
 Leu Lys Arg Lys Ala Glu Glu Asp Pro Glu Ala Ala Asp Ser Gly Glu  
 210 215 220  
 Pro Gln Asn Lys Arg Thr Pro Asp Leu Pro Glu Glu Glu Tyr Val Lys  
 225 230 235 240  
 Glu Glu Ile Gln Glu Asn Glu Glu Ala Val Lys Lys Met Leu Val Glu  
 245 250 255  
 Ala Thr Arg Glu Phe Glu Glu Val Val Val Asp Glu Ser Pro Pro Asp  
 260 265 270  
 Phe Glu Ile His Ile Thr Met Cys Asp Asp Asp Pro Pro Thr Pro Glu  
 275 280 285  
 Glu Asp Ser Glu Thr Gln Pro Asp Glu Glu Glu Glu Glu Glu Glu  
 290 295 300  
 Lys Val Ser Gln Pro Glu Val Gly Ala Ala Ile Lys Ile Ile Arg Gln  
 305 310 315 320  
 Leu Met Glu Lys Phe Asn Leu Asp Leu Ser Thr Val Thr Gln Ala Phe  
 325 330 335  
 Leu Lys Asn Ser Gly Glu Leu Glu Ala Thr Ser Ala Phe Leu Ala Ser  
 340 345 350  
 Gly Gln Arg Ala Asp Gly Tyr Pro Ile Trp Ser Arg Gln Asp Asp Ile  
 355 360 365  
 Asp Leu Gln Lys Asp Asp Glu Asp Thr Arg Glu Ala Leu Val Lys Lys  
 370 375 380  
 Phe Gly Ala Gln Asn Val Ala Arg Arg Ile Glu Phe Arg Lys Lys  
 385 390 395

&lt;210&gt; 95

&lt;211&gt; 1427

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 95

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 attcagcaaa aactcccctg atacctcata ccaacaagct gctgctctcc tccataccta 660  
 cctacgaaat ctatctccct acgtcacttc cacacctcct gttcttggac ccctcactat 720

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<210> 96  
 <211> 129  
 <212> PRT  
 <213> Homo sapiens

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 <222> (104)

<220>  
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 <222> (115)

<400> 96  
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 Ser Leu Leu Glu Trp Ile Asp Asp Leu Leu Trp Gln Ser Thr Leu Gln  
 35 40 45  
 Phe Phe His Pro Asp Glu Val Leu Phe Phe Tyr Thr Tyr Ser Leu Ser  
 50 55 60  
 Tyr Ser Arg Ser Pro Ala Thr Leu Tyr Pro Ser Leu Ile Ile Ser Arg  
 65 70 75 80  
 Ile Pro Ser Thr Ser Pro Thr Pro Ser Ser Pro Ser Pro Ile Leu Pro  
 85 90 95  
 Met His Phe Pro Leu Phe Leu Xaa Leu Tyr Arg Cys Pro Cys Pro Ala  
 100 105 110  
 Ser Pro Xaa Gly Asn Phe Pro His Leu Pro Ile Pro Pro Asn Leu Phe  
 115 120 125

Gln

<210> 97  
 <211> 2482  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure

&lt;222&gt; (1663)

&lt;400&gt; 97

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&lt;210&gt; 98

&lt;211&gt; 413

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 98

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Leu Ile Asp Gly Ser Glu Met Glu Trp Asp Phe Met Trp His Leu Arg
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Lys Val Pro Arg Ile Val Ser Glu Arg Thr Phe His Leu Thr Ser Pro
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65

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 Tyr Leu Ser Tyr Glu Thr Val Phe Glu Asn Gly Thr Arg Thr Leu Thr  
 85 90 95  
 Arg Val Lys Val Gln Asp Leu Val Leu Glu Pro Thr Gln Asn Ile Thr  
 100 105 110  
 Thr Lys Gly Val Ser Val Arg Arg Lys Arg Gln Val Tyr Gly Thr Asp  
 115 120 125  
 Ser Arg Phe Ser Ile Leu Asp Lys Arg Phe Leu Thr Asn Phe Pro Phe  
 130 135 140  
 Ser Thr Ala Val Lys Leu Ser Thr Gly Cys Ser Gly Ile Leu Ile Ser  
 145 150 155 160  
 Pro Gln His Val Leu Thr Ala Ala His Cys Val His Asp Gly Lys Asp  
 165 170 175  
 Tyr Val Lys Gly Ser Lys Lys Leu Arg Val Gly Leu Leu Lys Met Arg  
 180 185 190  
 Asn Lys Ser Gly Gly Lys Lys Arg Arg Gly Ser Lys Arg Ser Arg Arg  
 195 200 205  
 Glu Ala Ser Gly Gly Asp Gln Arg Glu Gly Thr Arg Glu His Leu Gln  
 210 215 220  
 Glu Arg Ala Lys Gly Gly Arg Arg Arg Lys Lys Ser Gly Arg Gly Gln  
 225 230 235 240  
 Lys Ile Ala Glu Gly Arg Pro Ser Phe Gln Trp Thr Arg Val Lys Asn  
 245 250 255  
 Thr His Ile Pro Lys Gly Trp Ala Arg Gly Gly Met Gly Asp Ala Thr  
 260 265 270  
 Leu Asp Tyr Asp Tyr Ala Leu Leu Glu Leu Lys Arg Ala His Lys Lys  
 275 280 285  
 Lys Tyr Met Glu Leu Gly Ile Ser Pro Thr Ile Lys Lys Met Pro Gly  
 290 295 300  
 Gly Met Ile His Phe Ser Gly Phe Asp Asn Asp Arg Ala Asp Gln Leu  
 305 310 315 320  
 Val Tyr Arg Phe Cys Ser Val Ser Asp Glu Ser Asn Asp Leu Leu Tyr  
 325 330 335  
 Gln Tyr Cys Asp Ala Glu Ser Gly Ser Thr Gly Ser Gly Val Tyr Leu  
 340 345 350  
 Arg Leu Lys Asp Pro Asp Lys Lys Asn Trp Lys Arg Lys Ile Ile Ala  
 355 360 365  
 Val Tyr Ser Gly His Gln Trp Val Asp Val His Gly Val Gln Lys Asp  
 370 375 380

66

Tyr Asn Val Ala Val Arg Ile Thr Pro Leu Lys Tyr Ala Gln Ile Cys  
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Leu Trp Ile His Gly Asn Asp Ala Asn Cys Ala Tyr Gly  
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 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> (650)

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 tgggctcctg attaaggact caagcccwcc tatgctgctg cwccagggtw acaagactgc 240  
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 <213> Homo sapiens

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<222> (383)

68

&lt;400&gt; 100

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 20             25             30

Thr Met Leu Asn Gly Leu Leu Ile Lys Asp Ser Ser Pro Pro Met Leu
 35             40             45

Leu Xaa Gln Val Xaa Lys Thr Ala Xaa Xaa Asp Xaa Phe Xaa Tyr Gln
 50             55             60

Xaa Cys Phe Met Xaa Ser Val Phe Asp His Phe Pro Glu Ile Leu Phe
 65             70             75             80

Ile His Xaa Thr Tyr Asn Pro Arg Gly Lys Val Leu Tyr Xaa Phe Leu
 85             90             95

Val Asp Gly Pro Xaa Val Gln Leu Glu Gly Xaa Leu Ala Arg Ala Val
100             105             110

Tyr Phe Ala Ile Pro Ala Lys Glu Asp Thr Glu Gly Leu Ala Gln Met
115             120             125

Phe Gln Val Phe Lys Lys Phe Asn Pro Ala Trp Glu Arg Val Cys Thr
130             135             140

Ile Leu Val Asp Pro His Phe Leu Pro Leu Pro Ile Leu Ala Met Glu
145             150             155             160

Phe Pro Thr Ala Glu Val Leu Leu Ser Ala Phe His Ile Cys Lys Phe
165             170             175

Leu Gln Ala Lys Phe Tyr Gln Leu Ser Leu Glu Arg Pro Val Glu Arg
180             185             190

Xaa Leu Leu Thr Ser Leu Gln Ser Thr Met Cys Ser Ala Thr Ala Gly
195             200             205

Asn Leu Arg Lys Leu Tyr Thr Leu Leu Ser Asn Cys Ile Pro Pro Ala
210             215             220

Lys Leu Pro Glu Leu His Ser His Trp Leu Leu Asn Asp Arg Ile Trp
225             230             235             240

Leu Ala His Arg Trp Arg Ser Arg Ala Glu Ser Ser His Tyr Phe Gln
245             250             255

Ser Leu Glu Val Thr Thr His Ile Leu Ser Gln Phe Phe Gly Thr Thr
260             265             270

Pro Ser Glu Lys Gln Gly Met Ala Ser Leu Phe Arg Tyr Met Gln Gln
275             280             285

Asn Ser Ala Asp Lys Ala Asn Phe Asn Gln Gly Leu Cys Ala Gln Asn
290             295             300

Asn His Ala Pro Pro Asp Ile Ile Pro Glu Ser Pro Lys Leu Glu Gln
305             310             315             320

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69,

Leu Val Glu Ser His Ile Gln His Ser Leu Asn Ala Ile Cys Thr Gly  
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                   340                  345                  350  
 Thr His Leu Ile Gly Ser Gly Ser Glu Lys Met Asn Ile Gln Ile Leu  
                   355                  360                  365  
 Glu Asp Thr His Lys Val Gln Pro Xaa Pro Pro Ala Ser Cys Xaa Cys  
                   370                  375                  380  
 Tyr Phe Asn Gln Ala Phe His Leu Pro Cys Arg His Ile Leu Ala Met  
                   385                  390                  395                  400  
 Leu Ser Ala Arg Arg Gln Val Leu Gln Pro Asp Met Leu Pro Ala Gln  
                   405                  410                  415  
 Trp Thr Ala Gly Cys Ala Thr Ser Leu Asp Ser Ile Leu Gly Ser Lys  
                   420                  425                  430  
 Trp Ser Glu Thr Leu Asp Lys His Leu Ala Val Thr His Leu Thr Glu  
                   435                  440                  445  
 Glu Val Gly Gln Leu Leu Gln His Cys Thr Lys Glu Glu Phe Glu Arg  
                   450                  455                  460  
 Arg Tyr Ser Thr Leu Arg Glu Leu Ala Asp Ser Trp Ile Gly Pro Tyr  
                   465                  470                  475                  480  
 Glu Gln Val Gln Leu  
                   485

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 <212> DNA  
 <213> Homo sapiens

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 ctgaactatg cctccccgat aaccgcagtc agccggccac tgaatgagat ggtccttgacc 180  
 ccactgacag agcaggaggg ggaagcctac ctggagaagt gtggcagcgt gcggcggcac 240  
 acggtggcca atgcccactc ggacatccag ctgctggcca tggccaccat gatgcactcs 300  
 ggcctggggg aggaggccar cagtgagaac aagtkcctgc tctgcccacc carcttcccc 360  
 ccgccccacc sgcagtgtctc cagtkagccc aacatcacccg acaaccctga cggactggag 420  
 gagggggcca ggggcagcca ggagggtctg gagctgaact gtgcttccct cagctgagtc 480  
 gccacccttg ggcctttcca tctcctgttt tgcaaccagg atgrggaccc ctccatctcc 540  
 gtggattact gaggggggct cttgctttat gcgatgctgc cttatttccct ttaggggtact 600  
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 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 700

<210> 102  
 <211> 139  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> UNSURE  
 <222> (88)



<220>  
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 <222> (93)

<220>  
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<220>  
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<220>  
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 Pro Lys Val Thr Val Leu Asn Tyr Ala Ser Pro Ile Thr Ala Val Ser  
           20                  25                  30  
 Arg Pro Leu Asn Glu Met Val Leu Thr Pro Leu Thr Glu Gln Glu Gly  
           35                  40                  45  
 Glu Ala Tyr Leu Glu Lys Cys Gly Ser Val Arg Arg His Thr Val Ala  
           50                  55                  60  
 Asn Ala His Ser Asp Ile Gln Leu Leu Ala Met Ala Thr Met Met His  
           65                  70                  75                  80  
 Ser Gly Leu Gly Glu Glu Ala Xaa Ser Glu Asn Lys Xaa Leu Leu Leu  
           85                  90                  95  
 Pro Pro Xaa Phe Pro Pro Pro His Xaa Gln Cys Ser Ser Xaa Pro Asn  
           100                  105                  110  
 Ile Thr Asp Asn Pro Asp Gly Leu Glu Glu Gly Ala Arg Gly Ser Gln  
           115                  120                  125  
 Glu Gly Ser Glu Leu Asn Cys Ala Ser Leu Ser  
           130                  135

<210> 103  
 <211> 658  
 <212> DNA  
 <213> Homo sapiens

<400> 103  
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 gcagtggccc atcagggtgg tgtctacaag ggaactttgg tccatctctc ttcagtgact 180  
 ggaggagccc ctggccagca tccttccaca castgctgct tgcaggcaca ggactggccc 240  
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 ggggtgcaacc ctactggtt tttgccccat ttttatgttc cattcatttc actgggattc 540  
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71,

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 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> UNSURE  
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&lt;400&gt; 104

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Val Ala His Gln Gly Gly Val Tyr Lys Gly Thr Leu Val His Leu Ser  
 20 25 30

Ser Val Thr Gly Gly Ala Pro Gly Gln His Pro Ser Thr Xaa Cys Cys  
 35 40 45

Leu Gln Ala Gln Asp Trp Pro Pro Pro Ser Arg Pro Pro Ala Trp Trp  
 50 55 60

Gln Ala Cys Leu Asn Leu Gly Val Pro Gln Gly Pro Leu Pro Asn Ala  
 65 70 75 80

Thr Glu Pro Gln Gln Gly Thr Arg Ile Lys Glu His Pro Thr Arg His  
 85 90 95

Pro Cys Leu Trp Pro Pro Pro Arg Val Ser Val Gly Phe Ser Gly Pro  
 100 105 110

Tyr Arg Pro Ser Ser Asn Pro Ala Pro Ser Ala Ser Pro Lys Glu Thr  
 115 120 125

Phe Leu Lys Phe Leu Glu Cys Gly Cys Asn Pro His Trp Phe Leu Pro  
 130 135 140

His Phe Tyr Val Pro Phe Ile Ser Leu Gly Phe  
 145 150 155

<210> 105  
 <211> 836  
 <212> DNA  
 <213> Homo sapiens

&lt;400&gt; 105

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 gtatcataga ataattcatc tcttgtcata tactttctcc cagttttgac ccagcaaaac 180  
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 aaagggggaa taaaccctta agtgggtggg actgtaactt tgtttgggga gacaaagagg 660  
 agactctctt gagaccttta ttatcaggat gaggtttaaa gtcagatccc aaggaaaaaa 720  
 cagccctagt gaaacttcca agctctttga gagttgactt tttggtttgg atagaaaaatg 780  
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72,

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 <211> 47  
 <212> PRT  
 <213> Homo sapiens

<400> 106  
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           20                    25                    30  
 Cys Val Tyr Ile Phe Arg Asn Gly Gly Asn Thr Leu Gly Ser Arg  
           35                    40                    45

<210> 107  
 <211> 1581  
 <212> DNA  
 <213> Homo sapiens

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 <212> PRT  
 <213> Homo sapiens

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           20                    25                    30

Glu Ser Ile Cys Leu Pro Val Leu Asp Gly Leu Leu His Trp Ala Val  
 35 40 45  
 Cys Pro Ser Ala Glu Ala Gln Asp Pro Phe Ser Thr Leu Gly Pro Asn  
 50 55 60  
 Ala Val Leu Ser Pro Gln Arg Leu Val Leu Glu Thr Leu Ser Lys Leu  
 65 70 75 80  
 Ser Ile Gln Asp Asn Asn Val Asp Leu Ile Leu Ala Thr Pro Pro Phe  
 85 90 95  
 Ser Arg Leu Glu Lys Leu Tyr Ser Thr Met Val Arg Phe Leu Ser Asp  
 100 105 110  
 Arg Lys Asn Pro Val Cys Arg Glu Met Ala Val Val Leu Leu Ala Asn  
 115 120 125  
 Leu Ala Gln Gly Asp Ser Leu Ala Ala Arg Ala Ile Ala Val Gln Lys  
 130 135 140  
 Gly Ser Ile Gly Asn Leu Leu Gly Phe Leu Glu Asp Ser Leu Ala Ala  
 145 150 155 160  
 Thr Gln Phe Gln Gln Ser Gln Ala Ser Leu Leu His Met Gln Asn Pro  
 165 170 175  
 Pro Phe Glu Pro Thr Ser Val Asp Met Met Arg Arg Ala Ala Arg Ala  
 180 185 190  
 Leu Leu Ala Leu Ala Lys Val Asp Glu Asn His Ser Glu Phe Thr Leu  
 195 200 205  
 Tyr Glu Ser Arg Leu Leu Asp Ile Ser Val Ser Pro Leu Met Asn Ser  
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&lt;210&gt; 109

&lt;211&gt; 1684

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 109

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atatctgcaa gatTTTTTTC atcaataaaa attatccttg raaaaaaaaa aaaaaaaaaa 1680
aaaa
1684

```

&lt;210&gt; 110

&lt;211&gt; 476

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 110

```

Met Val Gly Ala Met Trp Lys Val Ile Val Ser Leu Val Leu Leu Met
  1              5              10              15

```

```

Pro Gly Pro Cys Asp Gly Leu Phe His Ser Leu Tyr Arg Ser Val Ser
      20              25              30

```

```

Met Pro Pro Lys Gly Asp Ser Gly Gln Pro Leu Phe Leu Thr Pro Tyr
  35              40              45

```

```

Ile Glu Ala Gly Lys Ile Gln Lys Gly Arg Glu Leu Ser Leu Val Gly
  50              55              60

```

```

Pro Phe Pro Gly Leu Asn Met Lys Ser Tyr Ala Gly Phe Leu Thr Val
  65              70              75              80

```

```

Asn Lys Thr Tyr Asn Ser Asn Leu Phe Phe Trp Phe Phe Pro Ala Gln
      85              90              95

```

```

Ile Gln Pro Glu Asp Ala Pro Val Val Leu Trp Leu Gln Gly Gly Pro
  100              105              110

```

```

Gly Gly Ser Ser Met Phe Gly Leu Phe Val Glu His Gly Pro Tyr Val
  115              120              125

```

```

Val Thr Ser Asn Met Thr Leu Arg Asp Arg Asp Phe Pro Trp Thr Thr
  130              135              140

```

```

Thr Leu Ser Met Leu Tyr Ile Asp Asn Pro Val Gly Thr Gly Phe Ser
  145              150              155              160

```

```

Phe Thr Asp Asp Thr His Gly Tyr Ala Val Asn Glu Asp Asp Val Ala
      165              170              175

```

```

Arg Asp Leu Tyr Ser Ala Leu Ile Gln Phe Phe Gln Ile Phe Pro Glu
  180              185              190

```

```

Tyr Lys Asn Asn Asp Phe Tyr Val Thr Gly Glu Ser Tyr Ala Gly Lys
  195              200              205

```

```

Tyr Val Pro Ala Ile Ala His Leu Ile His Ser Leu Asn Pro Val Arg
  210              215              220

```

75.

Glu Val Lys Ile Asn Leu Asn Gly Ile Ala Ile Gly Asp Gly Tyr Ser  
 225 230 235 240  
 Asp Pro Glu Ser Ile Ile Gly Gly Tyr Ala Glu Phe Leu Tyr Leu Ile  
 245 250 255  
 Gly Leu Leu Asp Glu Lys Gln Lys Lys Tyr Phe Gln Lys Gln Cys His  
 260 265 270  
 Glu Cys Ile Glu His Ile Arg Lys Gln Asn Trp Phe Glu Ala Phe Glu  
 275 280 285  
 Ile Leu Asp Lys Leu Leu Asp Gly Asp Leu Thr Ser Asp Pro Ser Tyr  
 290 295 300  
 Phe Gln Asn Val Thr Gly Cys Ser Asn Tyr Tyr Asn Phe Leu Arg Cys  
 305 310 315 320  
 Thr Glu Pro Glu Asp Gln Leu Tyr Tyr Val Lys Phe Leu Ser Leu Pro  
 325 330 335  
 Glu Val Arg Gln Ala Ile His Val Gly Asn Gln Thr Phe Asn Asp Gly  
 340 345 350  
 Thr Ile Val Glu Lys Tyr Leu Arg Glu Asp Thr Val Gln Ser Val Lys  
 355 360 365  
 Pro Trp Leu Thr Glu Ile Met Asn Asn Tyr Lys Val Leu Ile Tyr Asn  
 370 375 380  
 Gly Gln Leu Asp Ile Ile Val Ala Ala Ala Leu Thr Glu Arg Ser Leu  
 385 390 395 400  
 Met Gly Met Asp Trp Lys Gly Ser Gln Glu Tyr Lys Lys Ala Glu Lys  
 405 410 415  
 Lys Val Trp Lys Ile Phe Lys Ser Asp Ser Glu Val Ala Gly Tyr Ile  
 420 425 430  
 Arg Gln Ala Gly Asp Phe His Gln Val Ile Ile Arg Gly Gly Gly His  
 435 440 445  
 Ile Leu Pro Tyr Asp Gln Pro Leu Arg Ala Phe Asp Met Ile Asn Arg  
 450 455 460  
 Phe Ile Tyr Gly Lys Gly Trp Asp Pro Tyr Val Gly  
 465 470 475

&lt;210&gt; 111

&lt;211&gt; 750

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 111

acgatgtgtt gaccggctgc cgtttgagga ctttggtcac ccagactaga caccttctgt 60  
 gtcattgttt ggaaagctga aagggaagga cagctgtgcc ctctgggag ctcatgtgtc 120  
 cctggcgctg tgctagcttt cttttacagc tgtttacaga caaggcaggc ctgaggcaga 180  
 tggccactgc tcttgtgatg tttgctcaga ggaatatgaa cattttatatt ttgaaaaggg 240  
 atgatgtggt ttttgccagg tgtttataat taatccttta atattatggg tattaacctc 300  
 ttaaacaatga atgaattctt gattgtttta acacagtacc taagactaat gctttctgtg 360

76.

```

gacaccactg agctctgect caactccacc ctctgcgacc ggaggactat gcccctagta 420
actgctgtcg gtgtggacgc tgtgctggtt ctgttttcta aaggagcaga aggacaggtc 480
tctgagacag gatcgttgtc cctacaggag gaacagtggc cttgcttctt agacgggtctt 540
cactgtgtgt tttaaaacaa caacaacaac aacaacaaca taaaactctt ttgacctgta 600
acttaaagat cataaacttc aggcaataat attttctgtg taagctttta aaattatttt 660
tggggatcat agcttgtttt attttgtgct ataaaattaa cagtattaaa tgacttatat 720
tcttagaata aaaaaaaaaa aaaaaaaaaa

```

&lt;210&gt; 112

&lt;211&gt; 89

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 112

```

Met Val Ile Asn Leu Leu Asn Met Asn Glu Phe Leu Ile Val Leu Thr
  1             5             10             15

```

```

Gln Tyr Leu Arg Leu Met Leu Ser Val Asp Thr Thr Glu Leu Cys Leu
      20             25             30

```

```

Asn Ser Thr Leu Cys Asp Arg Arg Thr Met Pro Leu Val Thr Ala Val
    35             40             45

```

```

Gly Val Asp Ala Val Leu Val Leu Phe Ser Lys Gly Ala Glu Gly Gln
    50             55             60

```

```

Val Ser Glu Thr Gly Ser Leu Ser Leu Gln Glu Glu Gln Trp Pro Cys
    65             70             75             80

```

```

Phe Leu Asp Gly Leu His Cys Val Phe
      85

```

&lt;210&gt; 113

&lt;211&gt; 2156

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (1353)

&lt;400&gt; 113

```

aagtgatcta cctgcctggg cctcccaagg tgctgggatt acgggtgtga gccaccgcgc 60
ccagcctatt cttttttggt tgtgataatg gtcacctaag tggacatgag gtagtgtcat 120
gtgggtttga tttgcatgtc cctgataaat aatgatgttg accatctact catgtgcttg 180
ttggctatth gcatggcgtg tttggagaaa cgtctgttca agggcctttgc cttttttttt 240
tgagacagar tcttactccg ttgcccarg ctggagtkcg gtggtgaggg gtgcaactgca 300
acatccgcct tccaggttca agcgattctt gtgcctcagc ctcccaaaga gctgggatta 360
caaaagtgca gtttgcccat ttttaatcga ttttgttctt gagttggagt tttttgtata 420
ttcaggctgt taacccttta tgagatagat ggtttgcaca tagtctcttc cattctatag 480
gatatcattt ctgttaatag attcctttgc tgtgcagaaa ctttttagtt tgaggtcatt 540
ccatttgtct atttttactt tcgttgccct tgctgttggt gtcattgttca agaaatcatt 600
gccaaagacca atgtcgtgaa gtctttccct ttgttttctt ctaagggttt tacagtttca 660
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ggtctgtagg tctgtcttta tgtcagcacc atactggctg ttggactttt taattctttt 960
cttgacagtg gtaatttatt tgcttctttt tcttattagt ccttttgcc actttaaata 1020
attaattttg ttaattttta gttttctggt atttttagttc attaatctca ttgcttctt 1080
tatttattht tttatttttt ttgagatgga gtcttgctct gtcactcagg ctggagtgca 1140

```

77

```

gtggcacgat ctcagctcac tgcaacctcc acctcccagg ttcaagtgat tctcctgtct 1200
cagtctcctg agtagctggg attacaggca cttgccacca tgcccggcta attttttgta 1260
tttttttagta gagacggggg ttcgctgtgt tgcccgggct ggtttcaaac ttctgagctc 1320
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tatggtgatg tgtcttaagt cgtcccttag tctttttttt cctaatacgt ctgtcaaatt 1740
tcagagaacc atgttaaaat cccctattat tgtggttttg aagggtgttt ccagtgtttt 1800
tcttcatttt aattcttctt ctgtcgtgtg gcgcctgcag attccaggct gcttgacatg 1860
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caaaactaac aatggaacag gcggcaaacc tatgccaata tactagaaat tgcagattaa 1980
atagatgaaa tattctaaac tggagtttac ataatgaaca taagagtaat cagagaatct 2040
gactcatttt agatgtgtgt gtgtgtgtat atatatgtgt gtgtgtgtga aaaacattga 2100
ctataataaa aataatctcg agttcaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaa 2156

```

&lt;210&gt; 114

&lt;211&gt; 94

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 114

```

Met Val Met Cys Leu Lys Ser Ser Leu Ser Leu Phe Phe Pro Asn Gln
 1             5             10             15
Ser Val Lys Phe Gln Arg Thr Met Leu Lys Ser Pro Ile Ile Val Val
      20             25             30
Leu Lys Val Val Ser Ser Val Phe Pro Ser Phe Asn Ser Ser Ser Val
      35             40             45
Ala Val Arg Leu Gln Ile Pro Gly Cys Leu Thr Trp Val Pro Phe His
      50             55             60
Met Gly Val Ser Gln Gln Thr Ala Leu Gln Ile Val His Thr Phe Ser
      65             70             75             80
Lys Thr Asn Asn Gly Thr Gly Gly Lys Pro Met Pro Ile Tyr
      85             90

```

&lt;210&gt; 115

&lt;211&gt; 3941

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (2895)

&lt;400&gt; 115

```

cagacacaga gatcagaatt ccaggaaatg atcttccagt gcgttctggg tcagttatgg 60
tgactgtaaa taccgtcatc acagctggcc ctcaaaataa cgcaataata acatatttac 120
ataatgacat attatgactg taagtgcagt cagccccatc tggggctgag gcggggggccc 180
tgctgtgcac tctcccccca gctatcccac cgggccaggg gtgggcctca gggttgtgct 240
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gcagaggccg gtgacctggc gaggacttgc ccaggagatt ggagctcctt gcttctgcgc 360
cacgcggatg cccacgcctg gtctcagctg ggttggtggc tctgagtggt catctcgttg 420
ctgccatatt ttcttgcttc attgaatttc actgtgctcc agcctgggca acacagccgg 480
actctgtttc aaaaaaaaaa attttttttt tccaagatag gatggtagag aaaataacct 540

```



ctgccatgtc ctgctatgaa tacagctttg tattttctctc tctagttttg tcagtttttg 600  
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ccattgtttt catatatattg tttgggacat tttacttttt tctgttaacg cttaccctag 1020  
aaattagaaa tgacaccacg tattcttagc gaagtccagt tttcagcatt ttgtccttat 1080  
tggacaatag caaggatatt agaactgtgt ggttccgctg gcttccgtct tgagttatgt 1140  
gctgctattg tcggatatatt tgtcttagat gtactactt tccgtgttcat tgtggatgt 1200  
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&lt;210&gt; 116

&lt;211&gt; 70

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 116

Met Cys Cys Tyr Cys Arg Ile Phe Cys Leu Arg Cys Thr Tyr Phe Pro  
1 5 10 15

Val His Cys Gly Met Cys Asn Leu Arg Tyr Phe Glu Phe Ser Thr Phe  
20 25 30

Leu Leu Ser Leu Ser Leu Ile Thr Tyr Cys Phe Trp Asp Pro Pro His  
35 40 45

Arg Gly Ser His Ser Leu Ser Leu Glu His Thr Pro Leu Asp Phe Leu  
50 55 60

Glu Trp Gly Leu Leu Arg  
65 70

&lt;210&gt; 117

&lt;211&gt; 1779

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 117

ccaagttcca ggtctagaat tcaaattact aatttactgc ttctctctct ctaagcctca 60  
gctccctgat ctagaccatg agatttacag taggagagta ccatgtttat ccccaaatac 120  
ttaacagcta gggttttccc agactgaata ataataataa cttttttaaa attcagaagg 180  
tatcttcaag ttcttggtt gcttcttgta cattcaatat caaagaagag aaacacact 240  
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caccaaaatg agcatcagcc ttgctttcag aaagcaggga ccacatatat atgattttaa 360  
aaaaatctgc gatcaacttt tctctaaaaa acccaaatat gctggggtac agaaagatca 420  
atgcaaaagc aaaacatcct gtgcctgtcc tagaggtccc cagaggcagg atgccccgac 480  
tcagaaagaa actcctaagc tggcctggcc aaaggaggga agaaccagg gtgggtgtcg 540  
taactcatct aaaaataacg atgtcatcag gcagatgtgc cattgtgctg gggctgggtg 600  
gggtgtggcag gccaccttg ggtatgcaaa gctctgacag tgtttcactt gctaccctcg 660  
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aggagatgga ggttgcatg agctgagatg gcaccactgc actccagtct gggtgacaga 1740  
gcaagaccca gactcaaaaa aaaaaaaaaa aaaaaaaaaa 1779

&lt;210&gt; 118

&lt;211&gt; 109

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 118

80

Met Ser Ile Ser Leu Ala Phe Arg Lys Gln Gly Pro His Ile Tyr Asp  
 1 5 10 15  
 Leu Lys Lys Ile Cys Asp Gln Leu Phe Ser Lys Lys Pro Lys Tyr Ala  
 20 25 30  
 Gly Val Gln Lys Asp Gln Cys Lys Ser Lys Thr Ser Cys Ala Cys Pro  
 35 40 45  
 Arg Gly Pro Gln Arg Gln Asp Ala Pro Thr Gln Lys Glu Thr Pro Lys  
 50 55 60  
 Leu Ala Trp Pro Lys Gly Gly Arg Thr Gln Gly Gly Cys Arg Asn Ser  
 65 70 75 80  
 Ser Lys Asn Asn Asp Val Ile Arg Gln Met Cys His Cys Ala Gly Ala  
 85 90 95  
 Gly Trp Val Trp Gln Ala His Leu Gly Tyr Ala Lys Leu  
 100 105

<210> 119  
 <211> 1170  
 <212> DNA  
 <213> Homo sapiens

<400> 119  
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 taccagggtcc gcgtgagggg ttccgggggt ctgggcaggc acaatggcgt ctcgagcagg 120  
 cccgcgagcg gccggcaccg acggcagcga ctttcagcac cgggagcgcg tcgccatgca 180  
 ctaccagatg agtgtgaccc tcaagtatga aatcaagaag ctgatctacg tacatctggg 240  
 catatggctg ctgctgggtg ctaagatgag cgtgggacac ctgaggctct tgtcacatga 300  
 tcagggtggcc atgccctatc agtgggaata cccgtatttg ctgagcattt tgccctctct 360  
 cttgggcctt ctctcccttc cccgcaacaa cattaagctac ctggtgctct ccatgatcag 420  
 catgggactc ttttccatcg ctccactcat ttatggcagc atggagatgt tccctgctgc 480  
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 ctttgggggtg aagcctggac atcccatcga atgaaaggac actagtacag cggttccaaa 720  
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 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1170

<210> 120  
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 <212> PRT  
 <213> Homo sapiens

<400> 120  
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 1 5 10 15  
 Phe Gln His Arg Glu Arg Val Ala Met His Tyr Gln Met Ser Val Thr  
 20 25 30

81.

Leu Lys Tyr Glu Ile Lys Lys Leu Ile Tyr Val His Leu Val Ile Trp  
 35 40 45

Leu Leu Leu Val Ala Lys Met Ser Val Gly His Leu Arg Leu Leu Ser  
 50 55 60

His Asp Gln Val Ala Met Pro Tyr Gln Trp Glu Tyr Pro Tyr Leu Leu  
 65 70 75 80

Ser Ile Leu Pro Ser Leu Leu Gly Leu Leu Ser Phe Pro Arg Asn Asn  
 85 90 95

Ile Ser Tyr Leu Val Leu Ser Met Ile Ser Met Gly Leu Phe Ser Ile  
 100 105 110

Ala Pro Leu Ile Tyr Gly Ser Met Glu Met Phe Pro Ala Ala Gln Gln  
 115 120 125

Leu Tyr Arg His Gly Lys Ala Tyr Arg Phe Leu Phe Gly Phe Ser Ala  
 130 135 140

Val Ser Ile Met Tyr Leu Val Leu Val Leu Ala Val Gln Val His Ala  
 145 150 155 160

Trp Gln Leu Tyr Tyr Ser Lys Lys Leu Leu Asp Ser Trp Phe Thr Ser  
 165 170 175

Thr Gln Glu Lys Lys His Lys  
 180

&lt;210&gt; 121

&lt;211&gt; 1127

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 121

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&lt;210&gt; 122

&lt;211&gt; 140

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

82

&lt;400&gt; 122

Met Glu Pro Ser Pro Phe Gly Asp Val Ser Ser Arg Leu Thr Thr Glu  
 1 5 10 15

Gln Ile Leu Tyr Asn Ile Lys Gln Glu Tyr Lys Arg Met Gln Lys Arg  
 20 25 30

Arg His Leu Glu Thr Ser Phe Gln Gln Thr Asp Pro Cys Cys Thr Ser  
 35 40 45

Asp Ala Gln Pro His Ala Phe Leu Leu Ser Gly Pro Ala Ser Pro Gly  
 50 55 60

Thr Ser Ser Ala Ala Ser Ser Pro Leu Lys Lys Glu Gln Pro Leu Phe  
 65 70 75 80

Thr Leu Arg Gln Val Gly Met Ile Cys Glu Arg Leu Leu Lys Glu Arg  
 85 90 95

Glu Glu Lys Val Arg Glu Glu Tyr Glu Glu Ile Leu Asn Thr Lys Leu  
 100 105 110

Ala Glu Gln Tyr Asp Ala Phe Val Lys Phe Thr His Asp Gln Ile Met  
 115 120 125

Arg Arg Tyr Gly Glu Gln Pro Ala Ser Tyr Val Ser  
 130 135 140

&lt;210&gt; 123

&lt;211&gt; 806

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 123

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 cacagttaac ccattaactt catttgtttg gcctttttgc atttttgtgt gttcttcatg 660  
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 aaaaaaaaaa aaaaaaaaaa aaaaaa 806

&lt;210&gt; 124

&lt;211&gt; 55

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; UNSURE

&lt;222&gt; (46)

&lt;400&gt; 124

Met Val Arg Leu Cys Gln Ala Leu Leu Leu Leu Val Ala Thr Val Ala  
 1 5 10 15

83.

Leu Ala Ser Arg Arg Phe Gln Ala Trp Gly Ser Thr Lys Val Val Arg  
 20 25 30

Thr Phe Gln Asp Ile Pro Gln Asn Tyr Val Tyr Val Gln Xaa Ala Leu  
 35 40 45

Trp Phe Ala Ile Glu Gly Val  
 50 55

&lt;210&gt; 125

&lt;211&gt; 1783

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 125

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tgraaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaa 1783

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&lt;210&gt; 126

&lt;211&gt; 136

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; UNSURE

&lt;222&gt; (108)

&lt;400&gt; 126

Met Leu Phe Trp Leu Ala Tyr His Pro His Ile Pro Thr Pro His His  
 1 5 10 15

Arg Ile Leu Phe Ser Phe Leu Pro Ser Asn Ser Trp Leu Pro Arg Cys  
 20 25 30

Gln Leu Cys Ser Leu Cys Leu Gln Phe Lys Gly Ala Pro Trp Lys Lys  
 35 40 45

Cys Asn Asn Ser Leu Thr Cys Asp Trp Tyr Leu Thr Ala Thr Thr Pro  
 50 55 60

Gly Gln Gln Trp Leu Thr Val Asp Lys Asp Asn Phe Phe Leu Ser Pro  
 65 70 75 80

Lys Pro Asn Ser Leu His Gln Leu Pro Ser Gln Asp Ser Leu Ser Gly  
 85 90 95

Pro Tyr Arg Cys Arg Ser Gly Trp Gln Leu Pro Xaa Leu Gly Lys Arg  
 100 105 110

Lys Tyr Pro Ile Met Ala Thr Tyr Leu His Leu Gln Leu Leu Pro Val  
 115 120 125

His Pro Gln Ser Leu Leu Phe Val  
 130 135

&lt;210&gt; 127

&lt;211&gt; 3149

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 127

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&lt;210&gt; 128

&lt;211&gt; 380

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 128

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Met Leu Pro Gly Met Pro Arg Phe Gln Trp Leu Ser Phe Phe Ile Phe
  1             5             10             15

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Leu Asp Thr Leu Ser Leu Gly Ile His Leu Glu Lys Lys Asn Asp Asp
      20             25             30

```

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His Ser Ser Trp Arg Lys Val Leu Glu Lys Cys Gln Gly Val Val Asp
      35             40             45

```

```

Ile Pro Phe Arg Ser Lys Gly Met Ser Arg Leu Gly Glu Glu Val Asn
      50             55             60

```

```

Gly Glu Ala Thr Glu Ser Gln Gln Lys Pro Arg Asn Lys Lys Ser Lys
      65             70             75             80

```

```

Met Asp Gly Met Val Pro Gly Asn His Gln Gly Arg Asp Pro Arg Lys
      85             90             95

```

```

His Lys Arg Lys Pro Leu Gly Val Gly Tyr Ser Ala Arg Lys Ser Pro
      100            105            110

```

```

Leu Tyr Asp Asn Cys Phe Leu His Ala Pro Asp Gly Gln Pro Leu Cys
      115            120            125

```

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Thr Cys Asp Arg Arg Lys Ala Gln Trp Tyr Leu Asp Lys Gly Ile Gly
      130            135            140

```

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Glu Leu Val Ser Glu Glu Pro Phe Val Val Lys Leu Arg Phe Glu Pro
      145            150            155            160

```

```

Ala Gly Arg Pro Glu Ser Pro Gly Asp Tyr Tyr Leu Met Val Lys Glu
      165            170            175

```



Asn Leu Cys Val Val Cys Gly Lys Arg Asp Ser Tyr Ile Arg Lys Asn  
           180                          185                          190  
 Val Ile Pro His Glu Tyr Arg Lys His Phe Pro Ile Glu Met Lys Asp  
           195                          200                          205  
 His Asn Ser His Asp Val Leu Leu Leu Cys Thr Ser Cys His Ala Ile  
           210                          215                          220  
 Ser Asn Tyr Tyr Asp Asn His Leu Lys Gln Gln Leu Ala Lys Glu Phe  
           225                          230                          235                          240  
 Gln Ala Pro Ile Gly Ser Glu Glu Gly Leu Arg Leu Leu Glu Asp Pro  
                           245                          250                          255  
 Glu Arg Arg Gln Val Arg Ser Gly Ala Arg Ala Leu Leu Asn Ala Glu  
           260                          265                          270  
 Ser Leu Pro Thr His Arg Lys Glu Glu Leu Leu Gln Ala Leu Arg Glu  
           275                          280                          285  
 Phe Tyr Asn Thr Asp Val Val Thr Glu Glu Met Leu Gln Glu Ala Ala  
           290                          295                          300  
 Ser Leu Glu Thr Arg Ile Ser Asn Glu Asn Tyr Val Pro His Gly Leu  
           305                          310                          315                          320  
 Lys Val Val Gln Cys His Ser Gln Gly Gly Leu Arg Ser Leu Met Gln  
                           325                          330                          335  
 Leu Glu Ser Arg Trp Arg Gln His Phe Leu Asp Ser Met Gln Pro Lys  
           340                          345                          350  
 His Leu Pro Gln Gln Trp Ser Val Asp His Asn His Gln Lys Leu Leu  
           355                          360                          365  
 Arg Lys Phe Gly Glu Asp Leu Pro Ile Gln Leu Ser  
           370                          375                          380

&lt;210&gt; 129

&lt;211&gt; 1861

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 129

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a                                                                                   1861

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<210> 130  
 <211> 571  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> UNSURE  
 <222> (202)

<220>  
 <221> UNSURE  
 <222> (504)

<400> 130  
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 Leu Ala Asp Tyr Leu Thr Ser Ala Lys Phe Leu Leu Tyr Leu Gly His  
 20 25 30  
 Ser Leu Ser Thr Trp Gly Asp Arg Met Trp His Phe Ala Val Ser Val  
 35 40 45  
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 50 55 60  
 Gly Leu Val Val Ala Gly Ser Val Leu Val Leu Gly Ala Ile Ile Gly  
 65 70 75 80  
 Asp Trp Val Asp Lys Asn Ala Arg Leu Lys Val Ala Gln Thr Ser Leu  
 85 90 95  
 Val Val Gln Asn Val Ser Val Ile Leu Cys Gly Ile Ile Leu Met Met  
 100 105 110  
 Val Phe Leu His Lys His Glu Leu Leu Thr Met Tyr His Gly Trp Val  
 115 120 125  
 Leu Thr Ser Cys Tyr Ile Leu Ile Ile Thr Ile Ala Asn Ile Ala Asn  
 130 135 140  
 Leu Ala Ser Thr Ala Thr Ala Ile Thr Ile Gln Arg Asp Trp Ile Val  
 145 150 155 160

Val Val Ala Gly Glu Asp Arg Ser Lys Leu Ala Asn Met Asn Ala Thr  
 165 170 175  
 Ile Arg Arg Ile Asp Gln Leu Thr Asn Ile Leu Ala Pro Met Ala Val  
 180 185 190  
 Gly Gln Ile Met Thr Phe Gly Ser Pro Xaa Ile Gly Cys Gly Phe Ile  
 195 200 205  
 Ser Gly Trp Asn Leu Val Ser Met Cys Val Glu Tyr Val Leu Leu Trp  
 210 215 220  
 Lys Val Tyr Gln Lys Thr Pro Ala Leu Ala Val Lys Ala Gly Leu Lys  
 225 230 235 240  
 Glu Glu Glu Thr Glu Leu Lys Gln Leu Asn Leu His Lys Asp Thr Glu  
 245 250 255  
 Pro Lys Pro Leu Glu Gly Thr His Leu Met Gly Val Lys Asp Ser Asn  
 260 265 270  
 Ile His Glu Leu Glu His Glu Gln Glu Pro Thr Cys Ala Ser Gln Met  
 275 280 285  
 Ala Glu Pro Phe Arg Thr Phe Arg Asp Gly Trp Val Ser Tyr Tyr Asn  
 290 295 300  
 Gln Pro Val Phe Leu Ala Gly Met Gly Leu Ala Phe Leu Tyr Met Thr  
 305 310 315 320  
 Val Leu Gly Phe Asp Cys Ile Thr Thr Gly Tyr Ala Tyr Thr Gln Gly  
 325 330 335  
 Leu Ser Gly Ser Ile Leu Ser Ile Leu Met Gly Ala Ser Ala Ile Thr  
 340 345 350  
 Gly Ile Met Gly Thr Val Ala Phe Thr Trp Leu Arg Arg Lys Cys Gly  
 355 360 365  
 Leu Val Arg Thr Gly Leu Ile Ser Gly Leu Ala Gln Leu Ser Cys Leu  
 370 375 380  
 Ile Leu Cys Val Ile Ser Val Phe Met Pro Gly Ser Pro Leu Asp Leu  
 385 390 395 400  
 Ser Val Ser Pro Phe Glu Asp Ile Arg Ser Arg Phe Ile Gln Gly Glu  
 405 410 415  
 Ser Ile Thr Pro Thr Lys Ile Pro Glu Ile Thr Thr Glu Ile Tyr Met  
 420 425 430  
 Ser Asn Gly Ser Asn Ser Ala Asn Ile Val Pro Glu Thr Ser Pro Glu  
 435 440 445  
 Ser Val Pro Ile Ile Ser Val Ser Leu Leu Phe Ala Gly Val Ile Ala  
 450 455 460  
 Ala Arg Ile Gly Leu Trp Ser Phe Asp Leu Thr Val Thr Gln Leu Leu  
 465 470 475 480  
 Gln Glu Asn Val Ile Glu Ser Glu Arg Gly Ile Ile Asn Gly Val Gln  
 485 490 495

Asn Ser Met Asn Tyr Leu Leu Xaa Leu Leu His Phe Ile Met Val Ile  
500 505 510

Leu Ala Pro Asn Pro Glu Ala Phe Gly Leu Leu Val Leu Ile Ser Val  
515 520 525

Ser Phe Val Ala Met Gly His Ile Met Tyr Phe Arg Phe Ala Gln Asn  
530 535 540

Thr Leu Gly Asn Lys Leu Phe Ala Cys Gly Pro Asp Ala Lys Glu Val  
545 550 555 560

Arg Lys Glu Asn Gln Ala Asn Thr Ser Val Val  
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<210> 131

<211> 2157

<212> DNA

<213> Homo sapiens

<400> 131

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actatgatta cttttcttta taatttcctt tcagttaata cttattttat tttctgtttt 180
tatcatctag tcaactcgca aacttcacgc atttgtctaa atctactcaa tatattccag 240
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<210> 132

<211> 270

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 132

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Met Ile Pro Asn Leu Asp Leu Asn Leu Asp Arg Asp Leu Val Leu Pro
 1           5           10           15

Asp Val Ser Tyr Gln Val Glu Ser Ser Glu Glu Asp Gln Ser Gln Thr
      20           25           30

Met Asp Pro Gln Gly Gln Thr Leu Leu Leu Phe Leu Phe Val Asp Phe
      35           40           45

His Ser Ala Phe Pro Val Gln Gln Met Glu Ile Trp Gly Val Tyr Thr
      50           55           60

Leu Leu Thr Thr His Leu Asn Ala Ile Leu Val Glu Ser His Ser Val
      65           70           75           80

Val Gln Gly Ser Ile Gln Phe Thr Val Asp Lys Val Leu Glu Gln His
      85           90           95

His Gln Ala Ala Lys Ala Gln Gln Lys Leu Gln Ala Ser Leu Ser Val
      100          105          110

Ala Val Asn Ser Ile Met Ser Ile Leu Thr Gly Ser Thr Arg Ser Ser
      115          120          125

Phe Arg Lys Met Cys Leu Gln Thr Leu Gln Ala Ala Asp Thr Gln Glu
      130          135          140

Phe Arg Thr Lys Leu His Lys Val Phe Arg Glu Ile Thr Gln His Gln
      145          150          155          160

Phe Leu His His Cys Ser Cys Glu Val Lys Gln Leu Thr Leu Glu Lys
      165          170          175

Lys Asp Ser Ala Gln Gly Thr Glu Asp Ala Pro Asp Asn Ser Ser Leu
      180          185          190

Glu Leu Leu Ala Val Leu Lys Gln Pro Ser Gln Pro Thr Ala Ala Gly
      195          200          205

Val Gln Gln Leu Ser His Ser Val Thr Ser Arg Asp Ala Arg Tyr Gln
      210          215          220

Arg Ala Ser Arg Lys Gln Glu Ala Gln Glu Gly Gln Pro Pro His Arg
      225          230          235          240

Gly Asp Ala Ser Ser Ala Leu Cys Gln Gly Pro Glu Pro Val Arg Gly
      245          250          255

Arg Pro Ala Pro Pro Gly Ser His Arg Gly Pro Pro His Ser
      260          265          270

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&lt;210&gt; 133

&lt;211&gt; 1607

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 133

```

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ataacatctt cttttcttcg ctgagtgctg tttatgctct aagcatgggt ctccttgggt 180
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gattattctg cttccagtag gcatagctaa tctgaaacag atagaaaagc agctgaattc 720
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ctgttgagaa taataaatgc atgaaatacc ttaaaaaaaa aaaaaaa 1607

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&lt;210&gt; 134

&lt;211&gt; 217

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 134

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Met Val Leu Val Asn Thr Ile Tyr Phe Lys Gly Gln Trp Gln Asn Lys
 1             5             10            15

Phe Gln Val Arg Glu Thr Val Lys Ser Pro Phe Gln Leu Ser Glu Gly
 20             25            30

Lys Asn Val Thr Val Glu Met Met Tyr Gln Ile Gly Thr Phe Lys Leu
 35             40            45

Ala Phe Val Lys Glu Pro Gln Met Gln Val Leu Glu Leu Pro Tyr Val
 50             55            60

Asn Asn Lys Leu Ser Met Ile Ile Leu Leu Pro Val Gly Ile Ala Asn
 65             70            75            80

Leu Lys Gln Ile Glu Lys Gln Leu Asn Ser Gly Thr Phe His Glu Trp
 85             90            95

Thr Ser Ser Ser Asn Met Met Glu Arg Glu Val Glu Val His Leu Pro
100            105            110

Arg Phe Lys Leu Glu Ile Lys Tyr Glu Leu Asn Ser Leu Leu Lys Pro
115            120            125

Leu Gly Val Thr Asp Leu Phe Asn Gln Val Lys Ala Asp Leu Ser Gly
130            135            140

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92

Met Ser Pro Thr Lys Gly Leu Tyr Leu Ser Lys Ala Ile His Lys Ser  
 145 150 155 160

Tyr Leu Asp Val Ser Glu Glu Gly Thr Glu Ala Ala Ala Ala Thr Gly  
 165 170 175

Asp Ser Ile Ala Val Lys Ser Leu Pro Met Arg Ala Gln Phe Lys Ala  
 180 185 190

Asn His Pro Phe Leu Phe Phe Ile Arg His Thr His Thr Asn Thr Ile  
 195 200 205

Leu Phe Cys Gly Lys Leu Ala Ser Pro  
 210 215

<210> 135  
 <211> 1537  
 <212> DNA  
 <213> Homo sapiens

<400> 135  
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 aagatcatca ttaaaaaaca agatttatac aacaattact taggatgttt gtgatctgcc 960  
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 graaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa 1537

<210> 136  
 <211> 86  
 <212> PRT  
 <213> Homo sapiens

<400> 136  
 Met His Ala Cys Ala Gly Leu Gly Trp Ala Ala Gly Gly Arg Gly Ala  
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Gly Leu Gly Val Cys Ala Gln Leu Ile Thr Ala Met His Cys Thr Ala  
 20 25 30

93

His Val Pro Arg Ala Tyr Arg Asp Pro Thr Leu Phe Arg Ala Phe Leu  
 35 40 45

Pro Pro Ala Arg Ala Gln Leu Pro Pro Ala Trp Ala Asn Leu Leu Gln  
 50 55 60

Gly Ser Pro Arg Arg Met Gly Thr Arg Lys Ala Val Asp Pro His Leu  
 65 70 75 80

Gln Gly Ala Phe Pro Ala  
 85

&lt;210&gt; 137

&lt;211&gt; 1302

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 137

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gcctcaccce ggagatggag ctctcgaagg ccttctctgg ccagcggaca ctcctatctg 240
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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aa 1302

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&lt;210&gt; 138

&lt;211&gt; 339

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 138

Met Ser Asp Pro Ser Gln Leu Thr Gln Asn Val Cys Leu Thr Gln Glu  
 1 5 10 15

Met Glu Leu Ser Lys Ala Phe Ser Gly Gln Arg Thr Leu Leu Ser Ala  
 20 25 30

Ile Leu Ser Met Leu Ser Leu Ser Phe Ser Thr Thr Ser Leu Leu Ser  
 35 40 45

Asn Tyr Trp Phe Val Gly Thr Gln Lys Val Pro Lys Pro Leu Cys Glu  
 50 55 60

Lys Gly Leu Ala Ala Lys Cys Phe Asp Met Pro Val Ser Leu Asp Gly  
 65 70 75 80



Asp Thr Asn Thr Ser Thr Gln Glu Val Val Gln Tyr Asn Trp Glu Thr  
                     85                    90                    95  
 Gly Asp Asp Arg Phe Ser Phe Arg Ser Phe Arg Ser Gly Met Trp Leu  
                     100                    105                    110  
 Ser Cys Glu Glu Thr Val Glu Glu Pro Gly Glu Arg Cys Arg Ser Phe  
                     115                    120                    125  
 Ile Glu Leu Thr Pro Pro Ala Lys Arg Glu Ile Leu Trp Leu Ser Leu  
                     130                    135                    140  
 Gly Thr Gln Ile Thr Tyr Ile Gly Leu Gln Phe Ile Ser Phe Leu Leu  
                     145                    150                    155                    160  
 Leu Leu Thr Asp Leu Leu Leu Thr Gly Asn Pro Ala Cys Gly Leu Lys  
                     165                    170                    175  
 Leu Ser Ala Phe Ala Ala Val Ser Ser Val Leu Ser Gly Leu Leu Gly  
                     180                    185                    190  
 Met Val Ala His Met Met Tyr Ser Gln Val Phe Gln Ala Thr Val Asn  
                     195                    200                    205  
 Leu Gly Pro Glu Asp Trp Arg Pro His Val Trp Asn Tyr Gly Trp Ala  
                     210                    215                    220  
 Phe Tyr Met Ala Trp Leu Ser Phe Thr Cys Cys Met Ala Ser Ala Val  
                     225                    230                    235                    240  
 Thr Thr Phe Asn Thr Tyr Thr Arg Met Val Leu Glu Phe Lys Cys Lys  
                     245                    250                    255  
 His Ser Lys Ser Phe Lys Glu Asn Pro Asn Cys Leu Pro His His His  
                     260                    265                    270  
 Gln Cys Phe Pro Arg Arg Leu Ser Ser Ala Ala Pro Thr Val Gly Pro  
                     275                    280                    285  
 Leu Thr Ser Tyr His Gln Tyr His Asn Gln Pro Ile His Ser Val Ser  
                     290                    295                    300  
 Glu Gly Val Asp Phe Tyr Ser Glu Leu Arg Asn Lys Gly Phe Gln Arg  
                     305                    310                    315                    320  
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                     325                    330                    335  
 Glu Gln Cys

&lt;210&gt; 139

&lt;211&gt; 3184

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (1644)

&lt;400&gt; 139

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tccctgtttt tttttttctc ttacattctt ttttttttct ctgtttatac attagaacaa 1860
gataagattt gaaatacttc cttgcaaata atgtgcaact cccaaggtga aactcaaata 1920
gaaaaagtca tctctctggt agaaaggatg gctttcctgt aatgactata gagtaagagt 1980
ggcagcaatc tttccatgcc cttttcagca gaaggcacag aacagtagcg ggactgccat 2040
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tataaaggat tgtgtactga ctgaatacat ttaaaagaaa ctatgctatt ggtttttagg ttaagcttcc 3120
tgctatgaac agagataaca tatcttttta ctatgctatt ggtttttagg ttaagcttcc 3180
taatgcataa taaatttaca gtggttaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3184
aaaa

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&lt;210&gt; 140

&lt;211&gt; 454

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; UNSURE

&lt;222&gt; (442)

&lt;400&gt; 140

Met Leu Thr Val Leu His Glu Thr Phe Ser Gln His Thr Phe Leu Met  
 1 5 10 15

Asn Gly Leu Ile Gln Gly Val Lys Gly Leu Leu Ser Phe Leu Ser Ala  
 20 25 30

Pro Leu Ile Gly Ala Leu Ser Asp Val Trp Gly Arg Lys Pro Phe Leu  
 35 40 45

Leu Gly Thr Val Phe Phe Thr Cys Phe Pro Ile Pro Leu Met Arg Ile  
 50 55 60

Ser Pro Trp Trp Tyr Phe Ala Met Ile Ser Val Ser Gly Val Phe Ser  
 65 70 75 80

Val Thr Phe Ser Val Ile Phe Ala Tyr Val Ala Asp Val Thr Gln Glu  
 85 90 95

His Glu Arg Ser Thr Ala Tyr Gly Trp Val Ser Ala Thr Phe Ala Ala  
 100 105 110

Ser Leu Val Ser Ser Pro Ala Ile Gly Ala Tyr Leu Ser Ala Ser Tyr  
 115 120 125

Gly Asp Ser Leu Val Val Leu Val Ala Thr Val Val Ala Leu Leu Asp  
 130 135 140

Ile Cys Phe Ile Leu Val Ala Val Pro Glu Ser Leu Pro Glu Lys Met  
 145 150 155 160

Arg Pro Val Ser Trp Gly Ala Gln Ile Ser Trp Lys Gln Ala Asp Pro  
 165 170 175

Phe Ala Ser Leu Lys Lys Val Gly Lys Asp Ser Thr Val Leu Leu Ile  
 180 185 190

Cys Ile Thr Val Phe Leu Ser Tyr Leu Pro Glu Ala Gly Gln Tyr Ser  
 195 200 205

Ser Phe Phe Leu Tyr Leu Arg Gln Val Ile Gly Phe Gly Ser Val Lys  
 210 215 220

Ile Ala Ala Phe Ile Ala Met Val Gly Ile Leu Ser Ile Val Ala Gln  
 225 230 235 240

Thr Ala Phe Leu Ser Ile Leu Met Arg Ser Leu Gly Asn Lys Asn Thr  
 245 250 255

Val Leu Leu Gly Leu Gly Phe Gln Met Leu Gln Leu Ala Trp Tyr Gly  
 260 265 270

Phe Gly Ser Gln Ala Trp Met Met Trp Ala Ala Gly Thr Val Ala Ala  
 275 280 285

Met Ser Ser Ile Thr Phe Pro Ala Ile Ser Ala Leu Val Ser Arg Asn  
 290 295 300

97,

Ala Glu Ser Asp Gln Gln Gly Val Ala Gln Gly Ile Ile Thr Gly Ile  
305 310 315 320

Arg Gly Leu Cys Asn Gly Leu Gly Pro Ala Leu Tyr Gly Phe Ile Phe  
325 330 335

Tyr Met Phe His Val Glu Leu Thr Glu Leu Gly Pro Lys Leu Asn Ser  
340 345 350

Asn Asn Val Pro Leu Gln Gly Ala Val Ile Pro Gly Pro Pro Phe Leu  
355 360 365

Phe Gly Ala Cys Ile Val Leu Met Ser Phe Leu Val Ala Leu Phe Ile  
370 375 380

Pro Glu Tyr Ser Lys Ala Ser Gly Val Gln Lys His Ser Asn Ser Ser  
385 390 395 400

Ser Gly Ser Leu Thr Asn Thr Pro Glu Arg Gly Ser Asp Glu Asp Ile  
405 410 415

Glu Pro Leu Leu Gln Asp Ser Ser Ile Trp Glu Leu Ser Ser Phe Glu  
420 425 430

Glu Pro Gly Asn Gln Cys Thr Glu Leu Xaa Thr Arg Gln Lys Val Gly  
435 440 445

Phe Cys Ile Arg His Leu  
450

&lt;210&gt; 141

&lt;211&gt; 2481

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 141

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aggtctagaa ttcaatcggg aagaaggaaa agttcccttc tgctgtgaaa ctatttggca 60
agaggctgga gggcccaatg gctgcaaaat cgcaacccaa cattcccaa gccaagagtc 120
tagatggcgt caccaatgac agaaccgcat ctcaagggca gtggggccgt gcctgggagg 180
tggaactggt ttactggcg agcgtcatct tctactgct gttcgcccc ttcatcgct 240
actacttcat catggcttgt gaccaatata gctgcgccct gaccggccct gtggtggaca 300
tcgtcaccgg acatgctcgg ctctcggaca tctgggcca gactccacct ataacgagga 360
aagccgcccc gctctatacc ttgtgggtca ccttcagggt gcttctgtac acgtctctcc 420
ctgacttctg ccataagttt ctaccgggt acgtaggagg catccaggag ggggcccgtga 480
ctcctgcagg ggttgtgaac aagtatcaga tcaacggcct gcaagcctgg ctccctcacgc 540
acctgctctg gtttgcaaac gtcctatctc tgtcctggtt ctgcgccacc atcatcttcg 600
acaactggat cccactgctg tgggtgcgcca acatccttgg ctatgccgtc tccaccttcg 660
ccatggtcaa gggctacttc ttcccacca gcgccagaga ctgcaaattc acaggcaatt 720
tcttttataa ctacatgatg ggcacgcagt ttaaccctcg gatcggaag tggtttgact 780
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tctgcaggc catctacgtg attgacttct tctggaacga aacctggtag ctgaagacca 960
ttgacatctg ccatgaccac ttcggggtgt acctgggctg gggcgactgt gtctggctgc 1020
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cgcacgccgt gggcgtcctg ctgctgggct tgggtgggcta ctacatcttc cgggtggcca 1140
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ccaaggtcat cgagtgtctc tacacatcgg ccgacgggca gaggcaccac agcaagctgc 1260
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gcttgcccta ctgctgggct tgtggcggtg gccacctgct gccctacttc tacatcatct 1380
acatggccat cctgctgacc caccgctgcc tccgggaaga gcaccgctgc gccagcaagt 1440
acggccggga ctgggagcgc tacaccgccc cagtgcctta ccgctgctg cctggaatct 1500

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tctaaggggca cgccctaggg agaagccctg tggggctgtc aagagcgtgt tctgccaggt 1560
ccatggggggc tggcatccca gctccaactc gaggagcctc agtttcctca tctgtaaaact 1620
ggagagagacc cagcacttgg caggtgtcca gtacctaatac acgctctgtt ccttgctttt 1680
gccttcaagg gaattccgag tgtccagcac tgccgtattg ccagcacaga cggattttct 1740
ctaatacagtg tccctggggc aggaggatga cccagtcacc tttactagtc ctttgagac 1800
aatttacctg tattaggagc ccaggccacg ctacactctg cccacactgg tgagcaggag 1860
gtcttcccac gccctgtcat taggctgcat ttactcttgc taaataaaaag tgggagtggg 1920
gcgtgcgcgt tatccatgta ttgcctttca gctctagatc cccctcccct gcctgctctg 1980
cagtcgtggg tggggcccgt gcgcggttcc tccctggtag cgtgcacggg gttgaactgg 2040
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aggagtgtct tgcctggagt ctgcagacct cagagaggtc ccagcactgg ctgtggcctt 2160
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agaactcttt ttaaactcta tgctccgagt agagtccatc tttatattaa acttcccctg 2460
ttcaaataaa aaaaaaaaaa a 2481

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&lt;210&gt; 142

&lt;211&gt; 475

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 142

```

Met Ala Ala Lys Ser Gln Pro Asn Ile Pro Lys Ala Lys Ser Leu Asp
  1             5             10             15

Gly Val Thr Asn Asp Arg Thr Ala Ser Gln Gly Gln Trp Gly Arg Ala
  20             25             30

Trp Glu Val Asp Trp Phe Ser Leu Ala Ser Val Ile Phe Leu Leu Leu
  35             40             45

Phe Ala Pro Phe Ile Val Tyr Tyr Phe Ile Met Ala Cys Asp Gln Tyr
  50             55             60

Ser Cys Ala Leu Thr Gly Pro Val Val Asp Ile Val Thr Gly His Ala
  65             70             75             80

Arg Leu Ser Asp Ile Trp Ala Lys Thr Pro Pro Ile Thr Arg Lys Ala
  85             90             95

Ala Gln Leu Tyr Thr Leu Trp Val Thr Phe Gln Val Leu Leu Tyr Thr
 100             105             110

Ser Leu Pro Asp Phe Cys His Lys Phe Leu Pro Gly Tyr Val Gly Gly
 115             120             125

Ile Gln Glu Gly Ala Val Thr Pro Ala Gly Val Val Asn Lys Tyr Gln
 130             135             140

Ile Asn Gly Leu Gln Ala Trp Leu Leu Thr His Leu Leu Trp Phe Ala
 145             150             155             160

Asn Ala His Leu Leu Ser Trp Phe Ser Pro Thr Ile Ile Phe Asp Asn
 165             170             175

Trp Ile Pro Leu Leu Trp Cys Ala Asn Ile Leu Gly Tyr Ala Val Ser
 180             185             190

Thr Phe Ala Met Val Lys Gly Tyr Phe Phe Pro Thr Ser Ala Arg Asp
 195             200             205

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Cys Lys Phe Thr Gly Asn Phe Phe Tyr Asn Tyr Met Met Gly Ile Glu  
 210 215 220  
 Phe Asn Pro Arg Ile Gly Lys Trp Phe Asp Phe Lys Leu Phe Phe Asn  
 225 230 235 240  
 Gly Arg Pro Gly Ile Val Ala Trp Thr Leu Ile Asn Leu Ser Phe Ala  
 245 250 255  
 Ala Lys Gln Arg Glu Leu His Ser His Val Thr Asn Ala Met Val Leu  
 260 265 270  
 Val Asn Val Leu Gln Ala Ile Tyr Val Ile Asp Phe Phe Trp Asn Glu  
 275 280 285  
 Thr Trp Tyr Leu Lys Thr Ile Asp Ile Cys His Asp His Phe Gly Trp  
 290 295 300  
 Tyr Leu Gly Trp Gly Asp Cys Val Trp Leu Pro Tyr Leu Tyr Thr Leu  
 305 310 315 320  
 Gln Gly Leu Tyr Leu Val Tyr His Pro Val Gln Leu Ser Thr Pro His  
 325 330 335  
 Ala Val Gly Val Leu Leu Leu Gly Leu Val Gly Tyr Tyr Ile Phe Arg  
 340 345 350  
 Val Ala Asn His Gln Lys Asp Leu Phe Arg Arg Thr Asp Gly Arg Cys  
 355 360 365  
 Leu Ile Trp Gly Arg Lys Pro Lys Val Ile Glu Cys Ser Tyr Thr Ser  
 370 375 380  
 Ala Asp Gly Gln Arg His His Ser Lys Leu Leu Val Ser Gly Phe Trp  
 385 390 395 400  
 Gly Val Ala Arg His Phe Asn Tyr Val Gly Asp Leu Met Gly Ser Leu  
 405 410 415  
 Ala Tyr Cys Leu Ala Cys Gly Gly Gly His Leu Leu Pro Tyr Phe Tyr  
 420 425 430  
 Ile Ile Tyr Met Ala Ile Leu Leu Thr His Arg Cys Leu Arg Asp Glu  
 435 440 445  
 His Arg Cys Ala Ser Lys Tyr Gly Arg Asp Trp Glu Arg Tyr Thr Ala  
 450 455 460  
 Ala Val Pro Tyr Arg Leu Leu Pro Gly Ile Phe  
 465 470 475

&lt;210&gt; 143

&lt;211&gt; 1518

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 143

cttccccact ggctcttggt ttatgagttc cccttttaag gatctgttgt gacttaccta 60  
 tctgggctag tgacctcaga tgtctcagac tgagcatctt accactgttt ctgggtgata 120  
 cttcactca tggctctaac acatttgcac ttcctctcat ctgagagagt acagtcacgg 180

100

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ggcagagctt gcatagggat ccaggtgtta ctagtcttac tctggagctg gtccaactca 240
gtttcatggc acagaactag attaggtctc cactgcgcag tctgttttac tgcttaggga 300
aagccagctt ttctaccac acacgtttag tttgaagagt atctatTTTT ggaggggtct 360
ttgggaggtt gggcaggctt ctttggatcc cagatacatt tagagctttt tgcattaagt 420
gtgaggaaaa taacttctct ttgatgatgt tgatacacca tgtkggcacc ytggggcaca 480
gcgggtttagc tggggagatt ccattgagaat gaacccaaac tactcttctt tgctaggggtc 540
ctttaccac acagaggtga gcctttcagg ttcttcattt tgcttagttt cttcccttgt 600
ccttggcatt taagaggcat ccattgtgta gccagccaaa gccccctgaa ggagctggct 660
gctttaaagg atttacttgg gaggatgtca aatggctttg ccttctgcag acttcattta 720
ttttaatctt tttatggctc ctttctcttg ctttaaaaca ggattataag cacacagcag 780
gtactgacac ctgaagtctt actaaattcc tgtcctcagg ccatcctttt tctcctgaaa 840
cctggactcc aattttcaat gacgtttttg tttttctctt tcaagcctaa ctatgggaca 900
gctttacgag aaggaaaaag atgaagatgg attcctatat gtggcctaca gcggagagaa 960
cacttttggc ttctgagggc cattgctggg ctagggtgcac cgtaactgct tgtgtatctt 1020
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tctccaggaa acttgtcctt ctggaaatca tatkgaatga tattttotata tgaagtga 1260
gtaggtgcgg tattaaagt aaagggaagg tgatgcattt attctgggtt atgcttgaag 1320
tgttagatgg ctaagtatta aaattatcca aattaaatcc ttagcagtca gaacacttgc 1380
ttcactagaa tatgccaaact gccaatcatg ttggactgag ctaatttggt cctcttctg 1440
aaactattaa ggtaaataat taacaataaa aattctctta taaaggcaaa aaaaaaaaaa 1500
aaaaaaaaaa aaaaaaaaaa 1518

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&lt;210&gt; 144

&lt;211&gt; 55

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 144

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Met Val Leu Thr His Leu His Phe Leu Ser Ser Gln Arg Val Gln Ser
  1                      5                      10                      15

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Arg Gly Arg Ala Cys Ile Gly Ile Gln Val Leu Leu Val Leu Leu Trp
      20                      25                      30

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Ser Trp Ser Asn Ser Val Ser Trp His Arg Thr Arg Leu Gly Leu His
  35                      40                      45

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Cys Ala Val Cys Phe Thr Ala
  50                      55

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&lt;210&gt; 145

&lt;211&gt; 2097

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 145

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ctcttgagta cctggggctt gcagatgcat gccaccacac ccggctaatt tttttttttt 60
ttaaatagag atgggggtctt gttctgttgc ccargctgggt ctggaactcc tggcttcaat 120
cagtccctcc acctcagctt cccaaagctc tgggattata ggcatgagcc actgtacctg 180
tocacctgag aaattttcta agcctggatt cagtcttatg aaatataata ctttgaaatg 240
cacaataact ttgaaaatga aactcattgc ttttcatttc accaggagt actaactata 300
ataagcttta gagcaaattc tccttagata tgatttttgt tattattaga aacacatact 360
atcttgataa ctaaattttg ccaatcattc ttcttgacta gtggtcttta tatatacata 420
catatatata tatatatata tatatatata tatgaggaat tttccataag tgacttgaaa 480
aatacagaat gcactccatg gtaggtctgt tcagtgttat caggaatact gtttctcatc 540
ttcctttctt ggtgtccctt tgcaggggtt ggtttgcac attatgggtc cgtctggaga 600
caacaaagga aattctctca ttcaactctt cgtcattttg gggtgggaaa acttagcttg 660
gagcccaaga ttattgagga gttcaaatat gtgaaagcag aaatgcaaaa gcacggagaa 720
gaccccttct gccctttctc catcatcagc aatgccgtct ctaacatcat ttgctccttg 780

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101,

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tgctttggcc agcgctttga ttacactaat agtgagttca agaaaatgct tggttttatg 840
tcacgaggcc tagaaatctg tctgaacagt caagtcctcc tgggtcaacat atgcccttgg 900
ctttattacc ttcccttttg accatttaag gaattaagac aaattgaaaa ggatataacc 960
agtttcctta aaaaaatcat caaagaccat caagagtctc tggatagaga gaaccctcag 1020
gacttcatag acatgtacct tctccacatg gaagaggaga ggaaaaataa tagtaacagc 1080
agttttgatg aagagtactt attttatatc attggggatc tctttattgc tgggactgat 1140
accacaacta actctttgct ctggtgcctg ctgtatatgt cgctgaaccc cgatgtataa 1200
gaaaagggtt atgaagaaat tgaaagagtc attggcgcca accgagctcc ttccctcaca 1260
gacaaggccc agatgcccta cacagaagcc accatcatgg aagtgcagag gctaactgtg 1320
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attcctaaag gcacattgat cttacccaac ctgtggtcag tacatagaga cccagccatt 1440
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aaaaaagaaa cctttattcc ttttgggata gggaagcggg tgtgtatggg agaacaactg 1560
gcaaagatgg aattattcct aatgtttgtg agcctaagtc agagtctcgc atttgcttta 1620
cctgaggatt ctaagaagcc cctcctgast ggaagatttg gtctaacttt agccccacat 1680
ccatttaata taactatttc aaggagatga agagcatctc caagaagaga tggtaaaaag 1740
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caactcagtg gatccaagct gggctcagag gtcggaagga gggtagagca cactgggagg 1860
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gcttccaccg atgggccaat cttctcattt cttagtgcct cagacatccc atatgtaaaa 2040
tgagagtaat aaaacttggc ttctctctac ctctcagcac taaaaaaaaa aaaaaaa 2097

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&lt;210&gt; 146

&lt;211&gt; 398

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; UNSURE

&lt;222&gt; (379)

&lt;400&gt; 146

```

Val Leu Ser Gly Ile Leu Phe Leu Ile Phe Leu Ser Trp Cys Pro Phe
  1             5             10             15

Ala Gly Val Val Phe Ala His Tyr Gly Pro Val Trp Arg Gln Gln Arg
  20             25             30

Lys Phe Ser His Ser Thr Leu Arg His Phe Gly Leu Gly Lys Leu Ser
  35             40             45

Leu Glu Pro Lys Ile Ile Glu Glu Phe Lys Tyr Val Lys Ala Glu Met
  50             55             60

Gln Lys His Gly Glu Asp Pro Phe Cys Pro Phe Ser Ile Ile Ser Asn
  65             70             75             80

Ala Val Ser Asn Ile Ile Cys Ser Leu Cys Phe Gly Gln Arg Phe Asp
  85             90             95

Tyr Thr Asn Ser Glu Phe Lys Lys Met Leu Gly Phe Met Ser Arg Gly
 100             105             110

Leu Glu Ile Cys Leu Asn Ser Gln Val Leu Leu Val Asn Ile Cys Pro
 115             120             125

Trp Leu Tyr Tyr Leu Pro Phe Gly Pro Phe Lys Glu Leu Arg Gln Ile
 130             135             140

Glu Lys Asp Ile Thr Ser Phe Leu Lys Lys Ile Ile Lys Asp His Gln
 145             150             155             160

```



102

Glu Ser Leu Asp Arg Glu Asn Pro Gln Asp Phe Ile Asp Met Tyr Leu  
 165 170 175  
 Leu His Met Glu Glu Glu Arg Lys Asn Asn Ser Asn Ser Ser Phe Asp  
 180 185 190  
 Glu Glu Tyr Leu Phe Tyr Ile Ile Gly Asp Leu Phe Ile Ala Gly Thr  
 195 200 205  
 Asp Thr Thr Thr Asn Ser Leu Leu Trp Cys Leu Leu Tyr Met Ser Leu  
 210 215 220  
 Asn Pro Asp Val Gln Glu Lys Val His Glu Glu Ile Glu Arg Val Ile  
 225 230 235 240  
 Gly Ala Asn Arg Ala Pro Ser Leu Thr Asp Lys Ala Gln Met Pro Tyr  
 245 250 255  
 Thr Glu Ala Thr Ile Met Glu Val Gln Arg Leu Thr Val Val Val Pro  
 260 265 270  
 Leu Ala Ile Pro His Met Thr Ser Glu Asn Thr Val Leu Gln Gly Tyr  
 275 280 285  
 Thr Ile Pro Lys Gly Thr Leu Ile Leu Pro Asn Leu Trp Ser Val His  
 290 295 300  
 Arg Asp Pro Ala Ile Trp Glu Lys Pro Glu Asp Phe Tyr Pro Asn Arg  
 305 310 315 320  
 Phe Leu Asp Asp Gln Gly Gln Leu Ile Lys Lys Glu Thr Phe Ile Pro  
 325 330 335  
 Phe Gly Ile Gly Lys Arg Val Cys Met Gly Glu Gln Leu Ala Lys Met  
 340 345 350  
 Glu Leu Phe Leu Met Phe Val Ser Leu Met Gln Ser Phe Ala Phe Ala  
 355 360 365  
 Leu Pro Glu Asp Ser Lys Lys Pro Leu Leu Xaa Gly Arg Phe Gly Leu  
 370 375 380  
 Thr Leu Ala Pro His Pro Phe Asn Ile Thr Ile Ser Arg Arg  
 385 390 395

&lt;210&gt; 147

&lt;211&gt; 2504

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 147

gtcactgtga gtggagccca tgcctgggctc tgtgccctct gtgtctgtgc atgcgcgtgt 60  
 gtgtgtgggc gtgtgtgcat tgctggggcca gcttgaaggg aaggcccgtc atgtccctgc 120  
 actctgtttt gcaagatgcc aaaccccagt tctgatgggg ctccaacagc caggctgtgg 180  
 tcctttgacg ttcctcacct gttgcccaacc tatcccgtag tgaactgaaa cccaatgaa 240  
 gacagaactg tgccctgggga gatgcaatga ggtgagggtc gaactcatcc ttttatattt 300  
 cttttcaaga ttggatcaga gctcatctcc atccagtctt gtttctatga aggcttcaat 360  
 ctgtttccat gcaaatttgc taatcagagc ccagagctgc tgggtccctc atctccctca 420  
 tctattatag attgacttac agcagggaga gaatctcttt agctcattcc taatgggggtt 480  
 gggatcacia tatgggtctgg tccaatctgc atcttgttgt gtccaagac cctatctcct 540

```

ccccaacatt cttattgcct ttggctccca gtaaggaacg aattgggggc cagggaggag 600
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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaa 2504

```

&lt;210&gt; 148

&lt;211&gt; 66

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 148

Met Glu Arg Glu Pro Leu Cys Leu Trp Gln Tyr His Leu Glu Arg Ser  
 1 5 10 15

Thr Ser Tyr Leu Gln Ala Phe Ser Pro Gly Leu Leu Ile Val Ser Val  
 20 25 30

Pro Pro Phe Leu Ser Ser Leu Gln Met Pro Ser Arg Gly Tyr Leu Ile  
 35 40 45

Leu Val Leu Phe Leu Cys Gly Phe Leu Gly Ser Arg Asp Leu Glu Phe  
 50 55 60

Pro Phe  
 65

&lt;210&gt; 149

&lt;211&gt; 928

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 149

```

caagaccagt cttgccaaca taacaagaat ctgtctctat ataagaagat taagaattgg 60
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acttgggccc aggcattcca gcttatgatt tcagtgaagt atgatcaca cactgaattc 180
caacctaata gatggagaga gactatgtct ctaaaaataa aaaataaaga gattaggaac 240
tgtctgcact aagatgactt tactattcca agaaatcctt gcctaagaaa gtaaagttga 300
aattactttt ttgtcctgga aactttccga tctatgtatc tgtactcata cagcctcatc 360
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ttacctttca aggttggtt tataggtctt gcctcactgt atccagcaat ccaaacttta 480
ccctatccca gtcaggactg cacacctcat gttgaaagac ataccttaga accagactcc 540
ccaaagctta caaatatccc acccttgact ccctttcttg aggtactaa gattatgtga 600
agacagtcac cttccttact gcagtgaaga ataaacttgg tttttgttca tcagtaaacc 660
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ccatttataa aagactgatg aatctagtaa cataaaaata aactgcatga taaatatcat 780
aaacaaagtc aaaagacaac tgacaaccag gttaaaaaca tgctttcaac atatattaca 840
ggaaaagggc taatatctct aatatgtaaa taattgttag aaattaagag atcaagcacc 900
aagcaccatc tagaaaaaaa aaaaaaaa

```

&lt;210&gt; 150

&lt;211&gt; 88

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 150

```

Met Tyr Leu Tyr Ser Tyr Ser Leu Ile Gly Leu Asn Ser Leu Leu Phe
  1                      5                      10                      15

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```

Arg Thr Val Asp His Ser Thr Gly Phe Ser Ser Asp Cys Leu Pro Phe
      20                      25                      30

```

```

Lys Ala Gly Phe Ile Gly Leu Ala Ser Leu Tyr Pro Ala Ile Gln Thr
    35                      40                      45

```

```

Leu Pro Tyr Pro Ser Gln Asp Cys Thr Pro His Val Glu Arg His Thr
   50 *                      55                      60

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```

Leu Glu Pro Asp Ser Pro Lys Leu Thr Asn Ile Pro Pro Leu Thr Pro
   65                      70                      75                      80

```

```

Phe Ser Glu Ala Thr Lys Ile Met
      85

```

&lt;210&gt; 151

&lt;211&gt; 1343

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 151

```

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ggggagtgtt tgcgtttctt ctccgttttg cagtgaacaa catctcagaa aggtggagct 180
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tctcacaac gacaccacaa ctccggaaag tacaatgacc agcgggcagg cccgagcttc 480
caccagtc cccagggccc tggaggactc gggcccgggt aatatctcag tctcaatcac 540
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catcaccttc accctgccta cagcgtggag ctcatatgac tgcgacctcc acggtcactg 720
tgagcaggtg gtattcacag cctgcatgac cctcacggcc agccctgggg tgttccccgt 780
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105.

gatcttcaca actgccagag atgccaacac aaaatacgcc caagattaca atcctttctg 900  
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 catttcaagt gcctgtaact gatttgtaca tatttataaa aatctattcg gaaaaaaaaa 1320  
 aaaaaaaaaa aaaaaaaaaa aaa 1343

&lt;210&gt; 152

&lt;211&gt; 314

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 152

Met Phe Ser Ile Asn Pro Leu Glu Asn Leu Lys Val Tyr Ile Ser Ser  
 1 5 10 15

Arg Pro Pro Leu Val Val Phe Met Ile Ser Val Ser Ala Met Ala Ile  
 20 25 30

Ala Phe Leu Thr Leu Gly Tyr Phe Phe Lys Ile Lys Glu Ile Lys Ser  
 35 40 45

Pro Glu Met Ala Glu Asp Trp Asn Thr Phe Leu Leu Arg Phe Asn Asp  
 50 55 60

Leu Asp Leu Cys Val Ser Glu Asn Glu Thr Leu Lys His Leu Thr Asn  
 65 70 75 80

Asp Thr Thr Thr Pro Glu Ser Thr Met Thr Ser Gly Gln Ala Arg Ala  
 85 90 95

Ser Thr Gln Ser Pro Gln Ala Leu Glu Asp Ser Gly Pro Val Asn Ile  
 100 105 110

Ser Val Ser Ile Thr Leu Thr Leu Asp Pro Leu Lys Pro Phe Gly Gly  
 115 120 125

Tyr Ser Arg Asn Val Thr His Leu Tyr Ser Thr Ile Leu Gly His Gln  
 130 135 140

Ile Gly Leu Ser Gly Arg Glu Ala His Glu Glu Ile Asn Ile Thr Phe  
 145 150 155 160

Thr Leu Pro Thr Ala Trp Ser Ser Asp Asp Cys Ala Leu His Gly His  
 165 170 175

Cys Glu Gln Val Val Phe Thr Ala Cys Met Thr Leu Thr Ala Ser Pro  
 180 185 190

Gly Val Phe Pro Val Thr Val Gln Pro Pro His Cys Val Pro Asp Thr  
 195 200 205

Tyr Ser Asn Ala Thr Leu Trp Tyr Lys Ile Phe Thr Thr Ala Arg Asp  
 210 215 220

Ala Asn Thr Lys Tyr Ala Gln Asp Tyr Asn Pro Phe Trp Cys Tyr Lys  
 225 230 235 240

106,

Gly Ala Ile Gly Lys Val Tyr His Ala Leu Asn Pro Lys Leu Thr Val  
 245 250 255

Ile Val Pro Asp Asp Arg Ser Leu Ile Asn Leu His Leu Met His  
 260 265 270

Thr Ser Tyr Phe Leu Phe Val Met Val Ile Thr Met Phe Cys Tyr Ala  
 275 280 285

Val Ile Lys Gly Arg Pro Ser Lys Leu Arg Gln Ser Asn Pro Glu Phe  
 290 295 300

Cys Pro Glu Lys Val Ala Leu Ala Glu Ala  
 305 310

&lt;210&gt; 153

&lt;211&gt; 3343

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 153

```

tccgcgcgcg gggcgcgcggg cggagctgcc tgccgggtccc gcgcgcgcgcg tccgcactcc 60
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107.

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```

&lt;210&gt; 154

&lt;211&gt; 389

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 154

```

Met Trp Ile Lys Phe Ser Ser Asp Glu Glu Leu Glu Gly Leu Gly Phe
  1             5             10             15

```

```

Arg Ala Lys Tyr Ser Phe Ile Pro Asp Pro Asp Phe Thr Tyr Leu Gly
      20             25             30

```

```

Gly Ile Leu Asn Pro Ile Pro Asp Cys Gln Phe Glu Leu Ser Gly Ala
  35             40             45

```

```

Asp Gly Ile Val Arg Ser Ser Gln Val Glu Gln Glu Glu Lys Thr Lys
  50             55             60

```

```

Pro Gly Gln Ala Val Asp Cys Ile Trp Thr Ile Lys Ala Thr Pro Lys
  65             70             75             80

```

```

Ala Lys Ile Tyr Leu Arg Phe Leu Asp Tyr Gln Met Glu His Ser Asn
      85             90             95

```

```

Glu Cys Lys Arg Asn Phe Val Ala Val Tyr Asp Gly Ser Ser Ser Ile
  100            105            110

```

```

Glu Asn Leu Lys Ala Lys Phe Cys Ser Thr Val Ala Asn Asp Val Met
  115            120            125

```

```

Leu Lys Thr Gly Ile Gly Val Ile Arg Met Trp Ala Asp Glu Gly Ser
  130            135            140

```

```

Arg Leu Ser Arg Phe Arg Met Leu Phe Thr Ser Phe Val Glu Pro Pro
  145            150            155            160

```

```

Cys Thr Ser Ser Thr Phe Phe Cys His Ser Asn Met Cys Ile Asn Asn
  165            170            175

```

```

Ser Leu Val Cys Asn Gly Val Gln Asn Cys Ala Tyr Pro Trp Asp Glu
  180            185            190

```

```

Asn His Cys Lys Glu Lys Lys Lys Ala Gly Val Phe Glu Gln Ile Thr
  195            200            205

```

108,

Lys Thr His Gly Thr Ile Ile Gly Ile Thr Ser Gly Ile Val Leu Val  
 210 215 220  
 Leu Leu Ile Ile Ser Ile Leu Val Gln Val Lys Gln Pro Arg Lys Lys  
 225 230 235 240  
 Val Met Ala Cys Lys Thr Ala Phe Asn Lys Thr Gly Phe Gln Glu Val  
 245 250 255  
 Phe Asp Pro Pro His Tyr Glu Leu Phe Ser Leu Arg Asp Lys Glu Ile  
 260 265 270  
 Ser Ala Asp Leu Ala Asp Leu Ser Glu Glu Leu Asp Asn Tyr Gln Lys  
 275 280 285  
 Met Arg Arg Ser Ser Thr Ala Ser Arg Cys Ile His Asp His His Cys  
 290 295 300  
 Gly Ser Gln Ala Ser Ser Val Lys Gln Ser Arg Thr Asn Leu Ser Ser  
 305 310 315 320  
 Met Glu Leu Pro Phe Arg Asn Asp Phe Ala Gln Pro Gln Pro Met Lys  
 325 330 335  
 Thr Phe Asn Ser Thr Phe Lys Lys Ser Ser Tyr Thr Phe Lys Gln Gly  
 340 345 350  
 His Glu Cys Pro Glu Gln Ala Leu Glu Asp Arg Val Met Glu Glu Ile  
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 Pro Cys Glu Ile Tyr Val Arg Gly Arg Glu Asp Ser Ala Gln Ala Ser  
 370 375 380  
 Ile Ser Ile Asp Phe  
 385

<210> 155  
 <211> 2991  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> (1270)

<220>  
 <221> unsure  
 <222> (2613)

<400> 155  
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 taacttcatt gagggtgctg gcacagaaga attacttcaa ctttttggat aaaatcggtc 180  
 aaaaggttct ttgattaagc gaggattgtg gtggtcatca agaacctttt cccgattgaa 240  
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aaagttttta ttgagccccc gaaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 2991

```

&lt;210&gt; 156

&lt;211&gt; 95

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 156

```

Met Asp Phe Ala Ala Ser Ile Glu Ala Met Trp Leu His Cys Leu Pro
  1             5             10             15

```

```

Ile Ser Gln Thr Val Leu Ser Gly Gly Pro Ser Ile Thr Ser Met Gln
      20             25             30

```

```

Val Glu Gly Lys Asn Ser Ile Ile Leu Thr Phe Arg Gln Leu Met Ala
      35             40             45

```

```

Glu Glu Gly Pro Trp Gly Leu Met Lys Gly Leu Ser Ala Arg Ile Ile
      50             55             60

```

```

Ser Ala Thr Pro Ser Thr Ile Val Ile Val Val Gly Tyr Glu Ser Leu
      65             70             75             80

```



110.

Lys Lys Leu Ser Leu Arg Pro Glu Leu Val Asp Ser Arg His Trp  
85 90 95

```
<210> 157
<211> 2293
<212> DNA
<213> Homo sapiens
```

<400> 157						
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cactgtggtg	ggcactgcag	tgggcctctc	ctcccacccc	cgagctctca	gccactccct	240
agcactcaca	gggactcccg	gtgcaagggg	cacaagtttg	cacacagtg	cctggctttg	300
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aaaaaaaaaa	aaa					2293

```
<210> 158
<211> 586
<212> PRT
<213> Homo sapiens
```

<220>  
<221> UNSURE  
<222> (286)

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<400> 158
Met  Pro  Leu  Leu  Lys  Met  Pro  Pro  Pro  Phe  Ser  Gly  Cys  Ser  His  Pro
  1          5          10          15
```

111,

Cys Ser Gly His Cys Gly Gly His Cys Ser Gly Pro Leu Leu Pro Pro  
 20 25 30  
 Pro Ser Ser Gln Pro Leu Pro Ser Thr His Arg Asp Pro Gly Cys Lys  
 35 40 45  
 Gly His Lys Phe Ala His Ser Gly Leu Ala Cys Gln Leu Pro Gln Pro  
 50 55 60  
 Cys Glu Ala Asp Glu Gly Leu Gly Glu Glu Glu Asp Ser Ser Ser Glu  
 65 70 75 80  
 Arg Ser Ser Cys Thr Ser Ser Ser Thr His Gln Arg Asp Gly Lys Phe  
 85 90 95  
 Cys Asp Cys Cys Tyr Cys Glu Phe Phe Gly His Asn Ala Pro Pro Ala  
 100 105 110  
 Ala Pro Thr Ser Arg Asn Tyr Thr Glu Ile Arg Glu Lys Leu Arg Ser  
 115 120 125  
 Arg Leu Thr Arg Arg Lys Glu Glu Leu Pro Met Lys Gly Gly Thr Leu  
 130 135 140  
 Gly Gly Ile Pro Gly Glu Pro Ala Val Asp His Arg Asp Val Asp Glu  
 145 150 155 160  
 Leu Leu Glu Phe Ile Asn Ser Thr Glu Pro Lys Val Pro Asn Ser Ala  
 165 170 175  
 Arg Ala Ala Lys Arg Ala Arg His Lys Leu Lys Lys Lys Glu Lys Glu  
 180 185 190  
 Lys Ala Gln Leu Ala Ala Glu Ala Leu Lys Gln Ala Asn Arg Val Ser  
 195 200 205  
 Gly Ser Arg Glu Pro Arg Pro Ala Arg Glu Arg Leu Leu Glu Trp Pro  
 210 215 220  
 Asp Arg Glu Leu Asp Arg Val Asn Ser Phe Leu Ser Ser Arg Leu Gln  
 225 230 235 240  
 Glu Ile Lys Asn Thr Val Lys Asp Ser Ile Arg Ala Ser Phe Ser Val  
 245 250 255  
 Cys Glu Leu Ser Met Asp Ser Asn Gly Phe Ser Lys Glu Gly Ala Ala  
 260 265 270  
 Glu Pro Glu Pro Gln Ser Leu Pro Pro Ser Asn Leu Ser Xaa Ser Ser  
 275 280 285  
 Glu Gln Gln Pro Asp Ile Asn Leu Asp Leu Ser Pro Leu Thr Leu Gly  
 290 295 300  
 Ser Pro Gln Asn His Thr Leu Gln Ala Pro Gly Glu Pro Ala Pro Pro  
 305 310 315 320  
 Trp Ala Glu Met Arg Gly Pro His Pro Pro Trp Thr Glu Val Arg Gly  
 325 330 335

112

Pro Pro Pro Gly Ile Val Pro Glu Asn Gly Leu Val Arg Arg Leu Asn  
 340 345 350  
 Thr Val Pro Asn Leu Ser Arg Val Ile Trp Val Lys Thr Pro Lys Pro  
 355 360 365  
 Gly Tyr Pro Ser Ser Glu Glu Pro Ser Ser Lys Glu Val Pro Ser Cys  
 370 375 380  
 Lys Gln Glu Leu Pro Glu Pro Val Ser Ser Gly Gly Lys Pro Gln Lys  
 385 390 395 400  
 Gly Lys Arg Gln Gly Ser Gln Ala Lys Lys Ser Glu Ala Ser Pro Ala  
 405 410 415  
 Pro Arg Pro Pro Ala Ser Leu Glu Val Pro Ser Ala Lys Gly Gln Val  
 420 425 430  
 Ala Gly Pro Lys Gln Pro Gly Arg Val Leu Glu Leu Pro Lys Val Gly  
 435 440 445  
 Ser Cys Ala Glu Ala Gly Glu Gly Ser Arg Gly Ser Arg Pro Gly Pro  
 450 455 460  
 Gly Trp Ala Gly Ser Pro Lys Thr Glu Lys Glu Lys Gly Ser Ser Trp  
 465 470 475 480  
 Arg Asn Trp Pro Gly Glu Ala Lys Ala Arg Pro Gln Glu Gln Glu Ser  
 485 490 495  
 Val Gln Pro Pro Gly Pro Ala Arg Pro Gln Ser Leu Pro Gln Gly Lys  
 500 505 510  
 Gly Arg Ser Arg Arg Ser Arg Asn Lys Gln Glu Lys Pro Ala Ser Ser  
 515 520 525  
 Leu Asp Asp Val Phe Leu Pro Lys Asp Met Asp Gly Val Glu Met Asp  
 530 535 540  
 Glu Thr Asp Arg Glu Val Glu Tyr Phe Lys Arg Phe Cys Leu Asp Ser  
 545 550 555 560  
 Ala Lys Gln Thr Arg Gln Lys Val Ala Val Asn Trp Thr Asn Phe Ser  
 565 570 575  
 Leu Lys Lys Thr Thr Pro Ser Thr Ala Gln  
 580 585

&lt;210&gt; 159

&lt;211&gt; 1704

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 159

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 taattttgag ctgcctcttt gtagtcttaa aaggcaggag cttcgtgttg tgggtctgct 120  
 aaccgtagc tttccgtggg caagtcgtgt gtactcctcg ccattggtca gctccaaaca 180  
 cgcttctaca ctgataacaa gaaatatgcc gtagatgatg ttcccttctc aatccctgct 240  
 gcctctgaaa ttgccgacct tagtaacatc atcaataaac tactaaagga caaaaatgag 300  
 ttccacaaac atgtggagtt tgatttcctt attaagggcc agtttctgcg aatgcccttg 360  
 gacaaacaca tggaaatgga gaacatctca tcagaagaag ttgtggaaat agaatacgtg 420

113

```

gagaagtata ctgcacccca gccagagcaa tgcattgttcc atgatgactg gatcagttca 480
attaaagggg cagaggaatg gatcttgact gggtcttatg ataagacttc tgggatctgg 540
tccttggaag gaaagtcaat aatgacaatt gtgggacata cggatgttgt aaaagatgtg 600
gcctgggtga aaaaagatag tttgtcctgc ttattattga gtgcttctat ggatcagact 660
attctcttat gggagtggaa tgtagagaga aacaaagtga aagccctaca ctgctgtaga 720
ggctcatgctg gaagtgtaga ttctatagct gttgatggct caggaactaa attttgagc 780
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gacaaagttc tgagtgtaga ctggacagac acagggtctc ttctgagtgg aggagcagac 1380
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acatagatgc agatgcagaa agcagccttt tgaagtttat ataatgtttt cacccttcat 1560
aacagctaac gtatcacttt ttcttatttk gtatttataa taagataggt kgtgtttata 1620
aaatacaaac tgtggcatac attctctata caaacttgaa attaaactga gttttacatt 1680
tcttctttta aaaaaaaaaa aaaa 1704

```

&lt;210&gt; 160

&lt;211&gt; 423

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 160

```

Met Ala Gln Leu Gln Thr Arg Phe Tyr Thr Asp Asn Lys Lys Tyr Ala
  1                      5                      10                      15

Val Asp Asp Val Pro Phe Ser Ile Pro Ala Ala Ser Glu Ile Ala Asp
      20                      25                      30

Leu Ser Asn Ile Ile Asn Lys Leu Leu Lys Asp Lys Asn Glu Phe His
      35                      40                      45

Lys His Val Glu Phe Asp Phe Leu Ile Lys Gly Gln Phe Leu Arg Met
      50                      55                      60

Pro Leu Asp Lys His Met Glu Met Glu Asn Ile Ser Ser Glu Glu Val
      65                      70                      75                      80

Val Glu Ile Glu Tyr Val Glu Lys Tyr Thr Ala Pro Gln Pro Glu Gln
      85                      90                      95

Cys Met Phe His Asp Asp Trp Ile Ser Ser Ile Lys Gly Ala Glu Glu
      100                      105                      110

Trp Ile Leu Thr Gly Ser Tyr Asp Lys Thr Ser Arg Ile Trp Ser Leu
      115                      120                      125

Glu Gly Lys Ser Ile Met Thr Ile Val Gly His Thr Asp Val Val Lys
      130                      135                      140

Asp Val Ala Trp Val Lys Lys Asp Ser Leu Ser Cys Leu Leu Leu Ser
      145                      150                      155                      160

Ala Ser Met Asp Gln Thr Ile Leu Leu Trp Glu Trp Asn Val Glu Arg
      165                      170                      175

```

114

Asn Lys Val Lys Ala Leu His Cys Cys Arg Gly His Ala Gly Ser Val  
 180 185 190  
 Asp Ser Ile Ala Val Asp Gly Ser Gly Thr Lys Phe Cys Ser Gly Ser  
 195 200 205  
 Trp Asp Lys Met Leu Lys Ile Trp Ser Thr Val Pro Thr Asp Glu Glu  
 210 215 220  
 Asp Glu Met Glu Glu Ser Thr Asn Arg Pro Arg Lys Lys Gln Lys Thr  
 225 230 235 240  
 Glu Gln Leu Gly Leu Thr Arg Thr Pro Ile Val Thr Leu Ser Gly His  
 245 250 255  
 Met Glu Ala Val Ser Ser Val Leu Trp Ser Asp Ala Glu Glu Ile Cys  
 260 265 270  
 Ser Ala Ser Trp Asp His Thr Ile Arg Val Trp Asp Val Glu Ser Gly  
 275 280 285  
 Ser Leu Lys Ser Thr Leu Thr Gly Asn Lys Val Phe Asn Cys Ile Ser  
 290 295 300  
 Tyr Ser Pro Leu Cys Lys Arg Leu Ala Ser Gly Ser Thr Asp Arg His  
 305 310 315 320  
 Ile Arg Leu Trp Asp Pro Arg Thr Lys Asp Gly Ser Leu Val Ser Leu  
 325 330 335  
 Ser Leu Thr Ser His Thr Gly Trp Val Thr Ser Val Lys Trp Ser Pro  
 340 345 350  
 Thr His Glu Gln Gln Leu Ile Ser Gly Ser Leu Asp Asn Ile Val Lys  
 355 360 365  
 Leu Trp Asp Thr Arg Ser Cys Lys Ala Pro Leu Tyr Asp Leu Ala Ala  
 370 375 380  
 His Glu Asp Lys Val Leu Ser Val Asp Trp Thr Asp Thr Gly Leu Leu  
 385 390 395 400  
 Leu Ser Gly Gly Ala Asp Asn Lys Leu Tyr Ser Tyr Arg Tyr Ser Pro  
 405 410 415  
 Thr Thr Ser His Val Gly Ala  
 420

&lt;210&gt; 161

&lt;211&gt; 2302

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 161

cgttggcaag caattcacaa ggtgggggaca gacttgtact ttaacatgta gtccattcaa 60  
 gcaaacaact ttggactcta ctgatagatg aaagagcaaa tgatgactag tttagcctct 120  
 gcatatcaac aatataatgc agatcaagta taatgctcaa tattagtac atgagtatca 180  
 ctaaattaca tagaaccctg atgggggtttc ctgtgtcgta atccattaaa tcgggtggcca 240  
 gtgcttgctg ccgtgggttta gtgattgggt gttagaaata aaaactcagg tctatttctt 300  
 accagtcagt aacaattttt agagaatgta cttggtatat aatatatgga cttcaggaac 360  
 tttattgggg tgggggggta attttgcctt accctgttca ctttcagatg awtaggcttt 420

115

```

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aattaagtgg tttagtaaat aatgctatac cgaggtgctt gcattgtatt tcataatttt 600
gttacaaacc aaaattattt ttaatgagaa cagtcttggg ttcagaggtg tgatgccaga 660
atgtattttt gtactgttag gcccttgga cagataccgg tgctttctga aagatgaaag 720
aaatgcaatg ggtgctcttc atgcaagggt gcaaacctac caagaatgca taatagtctc 780
acttttcccc aataaagaga tgcgtgtgac tagttttgga cttttaacct taatgggggt 840
tgcattgtct ctattgttaa tcattgtcag ctgcagtac atgatccaca gtcctgcatt 900
tactgccttt cacttaatga ttttggacag gtttttagaga gccaggatgt tggctctggg 960
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cctattttct tatgctgtaa cttaccccca atctttatct ctggattttt actctttaaa 1980
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cgagaaggag tgggaaggagg aatgaacgtt tcattctcgt taataaaggc attatcctaa 2280
ttaaaaaaaa aaaaaaaaaa aa 2302

```

&lt;210&gt; 162

&lt;211&gt; 94

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 162

```

Met Pro Glu Cys Ile Phe Val Leu Leu Gly Pro Trp Asn Arg Tyr Arg
1           5           10          15

```

```

Cys Phe Leu Lys Asp Glu Arg Asn Ala Met Gly Ala Leu His Ala Arg
20           25           30

```

```

Leu Gln Thr Tyr Gln Glu Cys Ile Ile Val Ser Leu Phe Pro Asn Lys
35           40           45

```

```

Glu Met Arg Val Thr Ser Phe Gly Leu Leu Thr Leu Met Gly Val Ala
50           55           60

```

```

Cys Leu Leu Leu Leu Ile Ile Val Ser Cys Ser Asp Met Ile His Ser
65           70           75          80

```

```

Pro Ala Phe Thr Ala Phe His Leu Met Ile Leu Asp Arg Phe
85           90

```

&lt;210&gt; 163

&lt;211&gt; 1538

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 163

```

rcagcctgct gcgcgcccag ggggtcccgcg ggttttcggg cgcaggggtgg cccccgcggc 60
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ccccggacrg caagtacctg gcttcctgtg tccagtaccg gttagtgggc cgggatgtga 180
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cgtgctggag cccggacggg cgccacattc tcaacaccac ggaattccat ctgctggataa 420
ccgtctgggc cttgtgcaca aaatccgtgt cttacatcaa ataccgaaa gcttgtctgc 480
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cacagctggg actgggctgc ctctccttcc cgccgccccg ggccggggcc ggccctctcc 840
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ctgttaccga cagagcaaac ccgaaaatgg gcataggaat gctggcattt agtcctgaca 960
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acagcttcac caggagggtt tccactgtgg tggctctggat tcagtgtatt attctatatt 1440
tctatagcaa agcatttttg taaatatgta tggatataaaa ctgtagtttt attatttaaa 1500
ataaatactt gctgatttat aaaaaaaaaa aaaaaaaaaa 1538

```

&lt;210&gt; 164

&lt;211&gt; 415

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; UNSURE

&lt;222&gt; (20)

&lt;220&gt;

&lt;221&gt; UNSURE

&lt;222&gt; (65)

&lt;400&gt; 164

```

Met Asn Phe Ser Glu Val Phe Lys Leu Ser Ser Leu Leu Cys Lys Phe
 1             5             10             15

Ser Pro Asp Xaa Lys Tyr Leu Ala Ser Cys Val Gln Tyr Arg Leu Val
 20             25             30

Val Arg Asp Val Asn Thr Leu Gln Ile Leu Gln Leu Tyr Thr Cys Leu
 35             40             45

Asp Gln Ile Gln His Ile Glu Trp Ser Ala Asp Ser Leu Phe Ile Leu
 50             55             60

Xaa Ala Met Tyr Lys Arg Gly Leu Val Gln Val Trp Ser Leu Glu Gln
 65             70             75             80

Pro Glu Trp His Cys Lys Ile Asp Glu Gly Ser Ala Gly Leu Val Ala
 85             90             95

```

117

Ser Cys Trp Ser Pro Asp Gly Arg His Ile Leu Asn Thr Thr Glu Phe  
 100 105 110  
 His Leu Arg Ile Thr Val Trp Ser Leu Cys Thr Lys Ser Val Ser Tyr  
 115 120 125  
 Ile Lys Tyr Pro Lys Ala Cys Leu Gln Gly Ile Thr Phe Thr Arg Asp  
 130 135 140  
 Gly Arg Tyr Met Ala Leu Ala Glu Arg Arg Asp Cys Lys Asp Tyr Val  
 145 150 155 160  
 Ser Ile Phe Val Cys Ser Asp Trp Gln Leu Leu Arg His Phe Asp Thr  
 165 170 175  
 Asp Thr Gln Asp Leu Thr Gly Ile Glu Trp Ala Pro Asn Gly Cys Val  
 180 185 190  
 Leu Ala Val Trp Asp Thr Cys Leu Glu Val Arg Ile Leu Asn His Val  
 195 200 205  
 Thr Trp Lys Met Ile Thr Glu Phe Gly His Pro Ala Ala Ile Asn Asp  
 210 215 220  
 Pro Lys Ile Val Val Tyr Lys Glu Ala Glu Lys Ser Pro Gln Leu Gly  
 225 230 235 240  
 Leu Gly Cys Leu Ser Phe Pro Pro Pro Arg Ala Gly Ala Gly Pro Leu  
 245 250 255  
 Pro Ser Ser Glu Ser Lys Tyr Glu Ile Ala Ser Val Pro Val Ser Leu  
 260 265 270  
 Gln Thr Leu Lys Pro Val Thr Asp Arg Ala Asn Pro Lys Met Gly Ile  
 275 280 285  
 Gly Met Leu Ala Phe Ser Pro Asp Ser Tyr Phe Leu Ala Thr Arg Asn  
 290 295 300  
 Asp Asn Ile Pro Asn Ala Val Trp Val Trp Asp Ile Gln Lys Leu Arg  
 305 310 315 320  
 Leu Phe Ala Val Leu Glu Gln Leu Ser Pro Val Arg Ala Phe Gln Trp  
 325 330 335  
 Asp Pro Gln Gln Pro Arg Leu Ala Ile Cys Thr Gly Gly Ser Arg Leu  
 340 345 350  
 Tyr Leu Trp Ser Pro Ala Gly Cys Met Ser Val Gln Val Pro Gly Glu  
 355 360 365  
 Gly Asp Phe Ala Val Leu Ser Leu Cys Trp His Leu Ser Gly Asp Ser  
 370 375 380  
 Met Ala Leu Leu Ser Lys Asp His Phe Cys Leu Cys Phe Leu Glu Thr  
 385 390 395 400  
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 405 410 415

&lt;210&gt; 165



<211> 3178  
<212> DNA  
<213> Homo sapiens

<220>  
<221> unsure  
<222> (1653)

<220>  
<221> unsure  
<222> (1767)

<400> 165  
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tgagaatggt cattatgact tagagaatgc tacacgtgta ggttgctggt gtgtcctgaa 360  
tccacaggca taaagcactc cccattttcc tactgtaatg cagattctcc ggctcaagg 420  
ctagaatatt tgatcctaag atcaagacat catgcccttc gaatagtact gctctttgtt 480  
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119.

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&lt;210&gt; 166

&lt;211&gt; 67

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 166

Met Ile Asn Thr Phe Thr Tyr Met Val Val Cys Leu Ser Glu Leu Phe  
 1 5 10 15

Ser Pro Ile Tyr Ser Pro Ser Val Tyr Gly Ser Val His Phe Cys His  
 20 25 30

Thr Pro Gly Asn Pro Val Ile Leu Phe Leu Asn Ile Leu Leu Met Asp  
 35 40 45

Leu Cys Ser Cys Leu Asn Val Phe Asn Phe Gln Gln Asn Glu Pro His  
 50 55 60

Ser Leu Phe  
 65

&lt;210&gt; 167

&lt;211&gt; 2401

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 167

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 tgtcattagg ctaataggac agcacttgaa tggcttaggg ctcaaccaga ctgttgatct 180  
 cctcatgcaa gagtcaggat gtggtttaga acatccttct gctaccaa atccgaaatca 240  
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 gcattctcct catgctattg tgaggatgaa gtttttgcgt ctgcagcaga agtacctaga 360  
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 gttcccatgt tatacgcagc agatacttac ggagcattgt aatgaagtgt ggttctgtaa 780  
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120

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a

```

&lt;210&gt; 168

&lt;211&gt; 498

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 168

```

Met Gln Glu Ser Gly Cys Arg Leu Glu His Pro Ser Ala Thr Lys Phe
  1             5             10             15

```

```

Arg Asn His Val Met Glu Gly Asp Trp Asp Lys Ala Glu Asn Asp Leu
      20             25             30

```

```

Asn Glu Leu Lys Pro Leu Val His Ser Pro His Ala Ile Val Arg Met
  35             40             45

```

```

Lys Phe Leu Leu Leu Gln Gln Lys Tyr Leu Glu Tyr Leu Glu Asp Gly
  50             55             60

```

```

Lys Val Leu Glu Ala Leu Gln Val Leu Arg Cys Glu Leu Thr Pro Leu
  65             70             75             80

```

```

Lys Tyr Asn Thr Glu Arg Ile His Val Leu Ser Gly Tyr Leu Met Cys
      85             90             95

```

```

Ser His Ala Glu Asp Leu Arg Ala Lys Ala Glu Trp Glu Gly Lys Gly
  100            105            110

```

```

Thr Ala Ser Arg Ser Lys Leu Leu Asp Lys Leu Gln Thr Tyr Leu Pro
  115            120            125

```

```

Pro Ser Val Met Leu Pro Pro Arg Arg Leu Gln Thr Leu Leu Arg Gln
  130            135            140

```

```

Ala Val Glu Leu Gln Arg Asp Arg Cys Leu Tyr His Asn Thr Lys Leu
  145            150            155            160

```

```

Asp Asn Asn Leu Asp Ser Val Ser Leu Leu Ile Asp His Val Cys Ser
  165            170            175

```

```

Arg Arg Gln Phe Pro Cys Tyr Thr Gln Gln Ile Leu Thr Glu His Cys
  180            185            190

```

```

Asn Glu Val Trp Phe Cys Lys Phe Ser Asn Asp Gly Thr Lys Leu Ala
  195            200            205

```

```

Thr Gly Ser Lys Asp Thr Thr Val Ile Ile Trp Gln Val Asp Pro Asp
  210            215            220

```

121

Thr His Leu Leu Lys Leu Leu Lys Thr Leu Glu Gly His Ala Tyr Gly  
225 230 235 240

Val Ser Tyr Ile Ala Trp Ser Pro Asp Asp Asn Tyr Leu Val Ala Cys  
245 250 255

Gly Pro Asp Asp Cys Ser Glu Leu Trp Leu Trp Asn Val Gln Thr Gly  
260 265 270

Glu Leu Arg Thr Lys Met Ser Gln Ser His Glu Asp Ser Leu Thr Ser  
275 280 285

Val Ala Trp Asn Pro Asp Gly Lys Arg Phe Val Thr Gly Gly Gln Arg  
290 295 300

Gly Gln Phe Tyr Gln Cys Asp Leu Asp Gly Asn Leu Leu Asp Ser Trp  
305 310 315 320

Glu Gly Val Arg Val Gln Cys Leu Trp Cys Leu Ser Asp Gly Lys Thr  
325 330 335

Val Leu Ala Ser Asp Thr His Gln Arg Ile Arg Gly Tyr Asn Phe Glu  
340 345 350

Asp Leu Thr Asp Arg Asn Ile Val Gln Glu Asp His Pro Ile Met Ser  
355 360 365

Phe Thr Ile Ser Lys Asn Gly Arg Leu Ala Leu Leu Asn Val Ala Thr  
370 375 380

Gln Gly Val His Leu Trp Asp Leu Gln Asp Arg Val Leu Val Arg Lys  
385 390 395 400

Tyr Gln Gly Val Thr Gln Gly Phe Tyr Thr Ile His Ser Cys Phe Gly  
405 410 415

Gly His Asn Glu Asp Phe Ile Ala Ser Gly Ser Glu Asp His Lys Val  
420 425 430

Tyr Ile Trp His Lys Arg Ser Glu Leu Pro Ile Ala Glu Leu Thr Gly  
435 440 445

His Thr Arg Thr Val Asn Cys Val Ser Trp Asn Pro Gln Ile Pro Ser  
450 455 460

Met Met Ala Ser Ala Ser Asp Asp Gly Thr Val Arg Ile Trp Gly Pro  
465 470 475 480

Ala Pro Phe Ile Asp His Gln Asn Ile Glu Glu Glu Cys Ser Ser Met  
485 490 495

Asp Ser

<210> 169

<211> 1110

<212> DNA

<213> Homo sapiens

<400> 169

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122,

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agcgctacgg gaaaacactt tccttctcaa gtttttttct gtgttcttgg gaattatttt 480
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gccaggcaaa aaccagaagt tgaccagcag attgtaatct acacgaaagg ctgtgtgccc 780
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```

&lt;210&gt; 170

&lt;211&gt; 193

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 170

```

Met Ser Gly Lys His Tyr Lys Gly Pro Glu Val Ser Cys Cys Ile Lys
  1              5              10              15

Tyr Phe Ile Phe Gly Phe Asn Val Ile Phe Trp Phe Leu Gly Ile Thr
  20              25              30

Phe Leu Gly Ile Gly Leu Trp Ala Trp Asn Glu Lys Gly Val Leu Ser
  35              40              45

Asn Ile Ser Ser Ile Thr Asp Leu Gly Gly Phe Asp Pro Val Trp Leu
  50              55              60

Phe Leu Val Val Gly Gly Val Met Phe Ile Leu Gly Phe Ala Gly Cys
  65              70              75              80

Ile Gly Ala Leu Arg Glu Asn Thr Phe Leu Leu Lys Phe Phe Ser Val
  85              90              95

Phe Leu Gly Ile Ile Phe Phe Leu Glu Leu Thr Ala Gly Val Leu Ala
 100              105              110

Phe Val Phe Lys Asp Trp Ile Lys Asp Gln Leu Tyr Phe Phe Ile Asn
 115              120              125

Asn Asn Ile Arg Ala Tyr Arg Asp Asp Ile Asp Leu Gln Asn Leu Ile
 130              135              140

Asp Phe Thr Gln Glu Tyr Ile Pro Met Gln Val Glu Ser Asp Val Ala
 145              150              155              160

Phe His Ser Pro Ala Ala Leu Lys Ile Pro Gln Lys Met Ser Ser Thr
 165              170              175

Leu Ser Val Ala Met Met Pro Gly Lys Asn Gln Lys Leu Thr Ser Arg
 180              185              190

Leu

```

123

<210> 171  
 <211> 1621  
 <212> DNA  
 <213> Homo sapiens

<400> 171  
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 aaggtctgct aggcagcttc acagcctttt ctttcctctt ctctatcaga ggtctctttg 180  
 gaagcaataa tgatgactat aacaagaact tatcttgctt tgcaagattc ttccgccgtc 240  
 agagtttctg atttattttc tgggggttcca tgtatgccag ggagaaagag agagcgcgaa 300  
 agagagagga tgtctctctc agactggcac ctggcggtga agctggctga ccagccactt 360  
 actccaaagt ctattcttcg gttgccagag acagaactgg gagaatactc gctagggggc 420  
 tatagtattt catttctgaa gcagcttatt gctggcaaac tccaggagtc tgttccagac 480  
 cctgagctga ttgatctgat ctactgtggt cggaagctaa aagatgacca gacacttgac 540  
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 gagtctctgg atcagatcat tgtggccacc ccaggcctca gcagtgacct tattgctctt 780  
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 ctggccagca ctccggagag cagctctcac acaccgactc ctggcaccca gggtcattcc 1200  
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 ttgggaggga ctcatgaagg tgccctccatc tctcccttcc ccaatatacc tgatggtcaa 1560  
 ctctaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1620  
 a 1621

<210> 172  
 <211> 420  
 <212> PRT  
 <213> Homo sapiens

<400> 172  
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 Val Arg Val Ser Asp Leu Phe Ser Gly Val Pro Cys Met Pro Gly Arg  
 20 25 30  
 Lys Arg Glu Arg Glu Arg Glu Arg Met Ser Leu Ser Asp Trp His Leu  
 35 40 45  
 Ala Val Lys Leu Ala Asp Gln Pro Leu Thr Pro Lys Ser Ile Leu Arg  
 50 55 60  
 Leu Pro Glu Thr Glu Leu Gly Glu Tyr Ser Leu Gly Gly Tyr Ser Ile  
 65 70 75 80  
 Ser Phe Leu Lys Gln Leu Ile Ala Gly Lys Leu Gln Glu Ser Val Pro  
 85 90 95

124

Asp Pro Glu Leu Ile Asp Leu Ile Tyr Cys Gly Arg Lys Leu Lys Asp  
 100 105 110  
 Asp Gln Thr Leu Asp Phe Tyr Gly Ile Gln Pro Gly Ser Thr Val His  
 115 120 125  
 Val Leu Arg Lys Ser Trp Pro Glu Pro Asp Gln Lys Pro Glu Pro Val  
 130 135 140  
 Asp Lys Val Ala Ala Met Arg Glu Phe Arg Val Leu His Thr Ala Leu  
 145 150 155 160  
 His Ser Ser Ser Ser Tyr Arg Glu Ala Val Phe Lys Met Leu Ser Asn  
 165 170 175  
 Lys Glu Ser Leu Asp Gln Ile Ile Val Ala Thr Pro Gly Leu Ser Ser  
 180 185 190  
 Asp Pro Ile Ala Leu Gly Val Leu Gln Asp Lys Asp Leu Phe Ser Val  
 195 200 205  
 Phe Ala Asp Pro Asn Met Leu Asp Thr Leu Val Pro Ala His Pro Ala  
 210 215 220  
 Leu Val Asn Ala Ile Val Leu Val Leu His Ser Val Ala Gly Ser Ala  
 225 230 235 240  
 Pro Met Pro Gly Thr Asp Ser Ser Ser Arg Ser Met Pro Ser Ser Ser  
 245 250 255  
 Tyr Arg Asp Met Pro Gly Gly Phe Leu Phe Glu Gly Leu Ser Asp Asp  
 260 265 270  
 Glu Asp Asp Phe His Pro Asn Thr Arg Ser Thr Pro Ser Ser Ser Thr  
 275 280 285  
 Pro Ser Ser Arg Pro Ala Ser Leu Gly Tyr Ser Gly Ala Ala Gly Pro  
 290 295 300  
 Arg Pro Ile Thr Gln Ser Glu Leu Ala Thr Ala Leu Ala Leu Ala Ser  
 305 310 315 320  
 Thr Pro Glu Ser Ser Ser His Thr Pro Thr Pro Gly Thr Gln Gly His  
 325 330 335  
 Ser Ser Gly Thr Ser Pro Met Ser Ser Gly Val Gln Ser Gly Thr Pro  
 340 345 350  
 Ile Thr Asn Asp Leu Phe Ser Gln Ala Leu Gln His Ala Leu Gln Ala  
 355 360 365  
 Ser Gly Gln Pro Ser Leu Gln Ser Gln Trp Gln Pro Gln Leu Gln Gln  
 370 375 380  
 Leu Arg Asp Met Gly Ile Gln Asp Asp Glu Leu Ser Leu Arg Ala Leu  
 385 390 395 400  
 Gln Ala Thr Gly Gly Asp Ile Gln Ala Ala Leu Glu Leu Ile Phe Ala  
 405 410 415  
 Gly Gly Ala Pro  
 420

125

<210> 173  
 <211> 1534  
 <212> DNA  
 <213> Homo sapiens

<400> 173  
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 gacccatcct ttctcgtcgg aatacgtctt ggctgtgcta cgaagtgaac acaaaggggc 180  
 cctcaaggcc ccctttggac gcaaagatct ttccaggcca ggtgtattcc gaacttaagt 240  
 accaccaga gatgagattc ttccactggt tcagcaagtg gaggaagctg catcgtgacc 300  
 aggagtatga ggtcacctgg tacatatcct ggagcccctg cacaagtgt acaagggata 360  
 tggccacggt cctggccgag gaccogaagg ttaccctgac catcttcgtt gcccgcctct 420  
 actacttctg ggaccagat taccaggagg cgcttcgag cctgtgtcag aaaagagacg 480  
 gtccgcgtgc caccatgaag atcatgaatt atgacgaatt tcagcactgt tggagcaagt 540  
 tcgtgtacag ccaaagagag ctatttgagc cttggaataa totgcctaaa tattatata 600  
 tactgcacat catgctgggg gagattctca gacactcgat ggatccaccc acattcactt 660  
 tcaactttaa caatgaacct tgggtcagag gacggcatga gacttacctg tggtatgagg 720  
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 aagatcttct tccaagaaat gcaaacaggc tgttcaccac catctccagc tgatcacaga 1320  
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 tttgaatcaa aaatttatat atatttcaag aataaagtac taagattgtg ctcaaaaaaa 1440  
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1500  
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaa 1534

<210> 174  
 <211> 384  
 <212> PRT  
 <213> Homo sapiens

<400> 174  
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 20 25 30  
 Val Trp Leu Cys Tyr Glu Val Lys Thr Lys Gly Pro Ser Arg Pro Pro  
 35 40 45  
 Leu Asp Ala Lys Ile Phe Arg Gly Gln Val Tyr Ser Glu Leu Lys Tyr  
 50 55 60  
 His Pro Glu Met Arg Phe Phe His Trp Phe Ser Lys Trp Arg Lys Leu  
 65 70 75 80  
 His Arg Asp Gln Glu Tyr Glu Val Thr Trp Tyr Ile Ser Trp Ser Pro  
 85 90 95  
 Cys Thr Lys Cys Thr Arg Asp Met Ala Thr Phe Leu Ala Glu Asp Pro  
 100 105 110



126

Lys Val Thr Leu Thr Ile Phe Val Ala Arg Leu Tyr Tyr Phe Trp Asp  
 115 120 125  
 Pro Asp Tyr Gln Glu Ala Leu Arg Ser Leu Cys Gln Lys Arg Asp Gly  
 130 135 140  
 Pro Arg Ala Thr Met Lys Ile Met Asn Tyr Asp Glu Phe Gln His Cys  
 145 150 155 160  
 Trp Ser Lys Phe Val Tyr Ser Gln Arg Glu Leu Phe Glu Pro Trp Asn  
 165 170 175  
 Asn Leu Pro Lys Tyr Tyr Ile Leu Leu His Ile Met Leu Gly Glu Ile  
 180 185 190  
 Leu Arg His Ser Met Asp Pro Pro Thr Phe Thr Phe Asn Phe Asn Asn  
 195 200 205  
 Glu Pro Trp Val Arg Gly Arg His Glu Thr Tyr Leu Cys Tyr Glu Val  
 210 215 220  
 Glu Arg Met His Asn Asp Thr Trp Val Leu Leu Asn Gln Arg Arg Gly  
 225 230 235 240  
 Phe Leu Cys Asn Gln Ala Pro His Lys His Gly Phe Leu Glu Gly Arg  
 245 250 255  
 His Ala Glu Leu Cys Phe Leu Asp Val Ile Pro Phe Trp Lys Leu Asp  
 260 265 270  
 Leu Asp Gln Asp Tyr Arg Val Thr Cys Phe Thr Ser Trp Ser Pro Cys  
 275 280 285  
 Phe Ser Cys Ala Gln Glu Met Ala Lys Phe Ile Ser Lys Asn Lys His  
 290 295 300  
 Val Ser Leu Cys Ile Phe Thr Ala Arg Ile Tyr Asp Asp Gln Gly Arg  
 305 310 315 320  
 Cys Gln Glu Gly Leu Arg Thr Leu Ala Glu Ala Gly Ala Lys Ile Ser  
 325 330 335  
 Ile Met Thr Tyr Ser Glu Phe Lys His Cys Trp Asp Thr Phe Val Asp  
 340 345 350  
 His Gln Gly Cys Pro Phe Gln Pro Trp Asp Gly Leu Asp Glu His Ser  
 355 360 365  
 Gln Asp Leu Ser Gly Arg Leu Arg Ala Ile Leu Gln Asn Gln Glu Asn  
 370 375 380

&lt;210&gt; 175

&lt;211&gt; 3005

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (1407)

&lt;400&gt; 175

```

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gtggataaac aaaaagataa gaatggcgag agaattgatca caataagggg tggcacagaa 180
tcaacaagat atgcagttca actaatcaat gcaactcattc aagatcctgc taaggaactg 240
gaagacttga ttcttaaaaa tcatatcaga acacctgcca gcaccaaatac aattcatgct 300
aactttctcat ctggagtagg taccacagca gcttccagta aaaatgcatt tcctttgggt 360
gctccaactc ttgtaacttc acaggcaaca acgttatcta cgttccagcc cgctaataaa 420
cttaataaga atgttccaac aaatgtacgt tcttctttcc cagtttctct acccttagct 480
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ttcccagtgga gacctgtgaa tctgggaac acaaatagct ctccaaagca taataacaca 660
agccgtctac ctaaccagaa cgggactggt ttaccctcag agtctgctgg actagctact 720
gccagttgtc ctatcactgt ctcttctgta gttgctgcca gtcagcaact gtgtgtcact 780
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aaaaa 3005

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<210> 176  
 <211> 832  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> UNSURE  
 <222> (12)

<220>

128.

&lt;221&gt; UNSURE

&lt;222&gt; (449)

&lt;400&gt; 176

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Ala His Ile Asp Val Asp Lys Gln Lys Asp Lys Asn Gly Glu Arg Met  
 20 25 30

Ile Thr Ile Arg Gly Gly Thr Glu Ser Thr Arg Tyr Ala Val Gln Leu  
 35 40 45

Ile Asn Ala Leu Ile Gln Asp Pro Ala Lys Glu Leu Glu Asp Leu Ile  
 50 55 60

Pro Lys Asn His Ile Arg Thr Pro Ala Ser Thr Lys Ser Ile His Ala  
 65 70 75 80

Asn Phe Ser Ser Gly Val Gly Thr Thr Ala Ala Ser Ser Lys Asn Ala  
 85 90 95

Phe Pro Leu Gly Ala Pro Thr Leu Val Thr Ser Gln Ala Thr Thr Leu  
 100 105 110

Ser Thr Phe Gln Pro Ala Asn Lys Leu Asn Lys Asn Val Pro Thr Asn  
 115 120 125

Val Arg Ser Ser Phe Pro Val Ser Leu Pro Leu Ala Tyr Pro His Pro  
 130 135 140

His Phe Ala Leu Leu Ala Ala Gln Thr Met Gln Gln Ile Arg His Pro  
 145 150 155 160

Arg Leu Pro Met Ala Gln Phe Gly Gly Thr Phe Ser Pro Ser Pro Asn  
 165 170 175

Thr Trp Gly Pro Phe Pro Val Arg Pro Val Asn Pro Gly Asn Thr Asn  
 180 185 190

Ser Ser Pro Lys His Asn Asn Thr Ser Arg Leu Pro Asn Gln Asn Gly  
 195 200 205

Thr Val Leu Pro Ser Glu Ser Ala Gly Leu Ala Thr Ala Ser Cys Pro  
 210 215 220

Ile Thr Val Ser Ser Val Val Ala Ala Ser Gln Gln Leu Cys Val Thr  
 225 230 235 240

Asn Thr Arg Thr Pro Ser Ser Val Arg Lys Gln Leu Phe Ala Cys Val  
 245 250 255

Pro Lys Thr Ser Pro Pro Ala Thr Val Ile Ser Ser Val Thr Ser Thr  
 260 265 270

Cys Ser Ser Leu Pro Ser Val Ser Ser Ala Pro Ile Thr Ser Gly Gln  
 275 280 285

Ala Pro Thr Thr Phe Leu Pro Ala Ser Thr Ser Gln Ala Gln Leu Ser  
 290 295 300

Ser Gln Lys Met Glu Ser Phe Ser Ala Val Pro Pro Thr Lys Glu Lys  
 305 310 315 320  
 Val Ser Thr Gln Asp Gln Pro Met Ala Asn Leu Cys Thr Pro Ser Ser  
 325 330 335  
 Thr Ala Asn Ser Cys Ser Ser Ser Ala Ser Asn Thr Pro Gly Ala Pro  
 340 345 350  
 Glu Thr His Pro Ser Ser Ser Pro Thr Pro Thr Ser Ser Asn Thr Gln  
 355 360 365  
 Glu Glu Ala Gln Pro Ser Ser Val Ser Asp Leu Ser Pro Met Ser Met  
 370 375 380  
 Pro Phe Ala Ser Asn Ser Glu Pro Ala Pro Leu Thr Leu Thr Ser Pro  
 385 390 395 400  
 Arg Met Val Ala Ala Asp Asn Gln Asp Thr Ser Asn Leu Pro Gln Leu  
 405 410 415  
 Ala Val Pro Ala Pro Arg Val Ser His Arg Met Gln Pro Arg Gly Ser  
 420 425 430  
 Phe Tyr Ser Met Val Pro Asn Ala Thr Ile His Gln Asp Pro Gln Ser  
 435 440 445  
 Xaa Phe Val Thr Asn Pro Val Thr Leu Thr Pro Pro Gln Gly Pro Pro  
 450 455 460  
 Ala Ala Val Gln Leu Ser Ser Ala Val Asn Ile Met Asn Gly Ser Gln  
 465 470 475 480  
 Met His Ile Asn Pro Ala Asn Lys Ser Leu Pro Pro Thr Phe Gly Pro  
 485 490 495  
 Ala Thr Leu Phe Asn His Phe Ser Ser Leu Phe Asp Ser Ser Gln Val  
 500 505 510  
 Pro Ala Asn Gln Gly Trp Gly Asp Gly Pro Leu Ser Ser Arg Val Ala  
 515 520 525  
 Thr Asp Ala Ser Phe Thr Val Gln Ser Ala Phe Leu Gly Asn Ser Val  
 530 535 540  
 Leu Gly His Leu Glu Asn Met His Pro Asp Asn Ser Lys Ala Pro Gly  
 545 550 555 560  
 Phe Arg Pro Pro Ser Gln Arg Val Ser Thr Ser Pro Val Gly Leu Pro  
 565 570 575  
 Ser Ile Asp Pro Ser Gly Ser Ser Pro Ser Ser Ser Ser Ala Pro Leu  
 580 585 590  
 Ala Ser Phe Ser Gly Ile Pro Gly Thr Arg Val Phe Leu Gln Gly Pro  
 595 600 605  
 Ala Pro Val Gly Thr Pro Ser Phe Asn Arg Gln His Phe Ser Pro His  
 610 615 620  
 Pro Trp Thr Ser Ala Ser Asn Ser Ser Thr Ser Ala Pro Pro Thr Leu  
 625 630 635 640

Gly Gln Pro Lys Gly Val Ser Ala Ser Gln Asp Arg Lys Ile Pro Pro  
                   645                  650                  655  
 Pro Ile Gly Thr Glu Arg Leu Ala Arg Ile Arg Gln Gly Gly Ser Val  
                   660                  665                  670  
 Ala Gln Ala Pro Ala Gly Thr Ser Phe Val Ala Pro Val Gly His Ser  
                   675                  680                  685  
 Gly Ile Trp Ser Phe Gly Val Asn Ala Val Ser Glu Gly Leu Ser Gly  
                   690                  695                  700  
 Trp Ser Gln Ser Val Met Gly Asn His Pro Met His Gln Gln Leu Ser  
                   705                  710                  715                  720  
 Asp Pro Ser Thr Phe Ser Gln His Gln Pro Met Glu Arg Asp Asp Ser  
                   725                  730                  735  
 Gly Met Val Ala Pro Ser Asn Ile Phe His Gln Pro Met Ala Ser Gly  
                   740                  745                  750  
 Phe Val Asp Phe Ser Lys Gly Leu Pro Ile Ser Met Tyr Gly Gly Thr  
                   755                  760                  765  
 Ile Ile Pro Ser His Pro Gln Leu Ala Asp Val Pro Gly Gly Pro Leu  
                   770                  775                  780  
 Phe Asn Gly Leu His Asn Pro Asp Pro Ala Trp Asn Pro Met Ile Lys  
                   785                  790                  795                  800  
 Val Ile Gln Asn Ser Thr Glu Cys Thr Asp Ala Gln Gln Ile Trp Pro  
                   805                  810                  815  
 Gly Thr Trp Ala Pro His Ile Gly Asn Met His Leu Lys Tyr Val Asn  
                   820                  825                  830

<210> 177  
 <211> 1561  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> (1150)

<400> 177  
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 cctccctcgc ggctgggtga cagctgggtc cggctcgctc cgggctgcct ggggtgcgag 180  
 gatcgcgac cccgtcttcg cgcgctgtgc ctgccgcccc gccccctcgt cccgccccgc 240  
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 tcacaacaca ggtattacag gaataacgga agccgttaaa gagatcacac tggaaaataa 780  
 ggacaatata aggcttcaag attgctcagc actatgtgaa gaggaagaag atgaagatga 840

131

```

aggagaagct gcagatatgg aagaatatga agagagtgga ttgttggaag cagatgaggc 900
taccctagat acaaggaaaa tagtagaagc ttgtaaagcc aaaactgatg ctggcggtga 960
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gaattaaccc atagatgtga ccattgacca tattcatcaa tatatacagt ttctctaata 1440
agggaacttat atgtttatgc attaaataaa aatatgttcc actaccagcc ttatttgttt 1500
aataaaaatc agtgcaaaga gaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1560
a                                                                                   1561

```

&lt;210&gt; 178

&lt;211&gt; 314

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 178

```

Met Gln Asn Val Ile Asn Thr Val Lys Gly Lys Ala Leu Glu Val Ala
  1                      5                      10                      15

```

```

Glu Tyr Leu Thr Pro Val Leu Lys Glu Ser Lys Phe Lys Glu Thr Gly
      20                      25                      30

```

```

Val Ile Thr Pro Glu Glu Phe Val Ala Ala Gly Asp His Leu Val His
      35                      40                      45

```

```

His Cys Pro Thr Trp Gln Trp Ala Thr Gly Glu Glu Leu Lys Val Lys
      50                      55                      60

```

```

Ala Tyr Leu Pro Thr Gly Lys Gln Phe Leu Val Thr Lys Asn Val Pro
      65                      70                      75                      80

```

```

Cys Tyr Lys Arg Cys Lys Gln Met Glu Tyr Ser Asp Glu Leu Glu Ala
      85                      90                      95

```

```

Ile Ser Glu Glu Asp Asp Gly Asp Gly Gly Trp Val Asp Thr Tyr His
      100                      105                      110

```

```

Asn Thr Gly Ile Thr Gly Ile Thr Glu Ala Val Lys Glu Ile Thr Leu
      115                      120                      125

```

```

Glu Asn Lys Asp Asn Ile Arg Leu Gln Asp Cys Ser Ala Leu Cys Glu
      130                      135                      140

```

```

Glu Glu Glu Asp Glu Asp Glu Gly Glu Ala Ala Asp Met Glu Glu Tyr
      145                      150                      155                      160

```

```

Glu Glu Ser Gly Leu Leu Glu Thr Asp Glu Ala Thr Leu Asp Thr Arg
      165                      170                      175

```

```

Lys Ile Val Glu Ala Cys Lys Ala Lys Thr Asp Ala Gly Gly Glu Asp
      180                      185                      190

```

```

Ala Ile Leu Gln Thr Arg Thr Tyr Asp Leu Tyr Ile Thr Tyr Asp Lys
      195                      200                      205

```

```

Tyr Tyr Gln Thr Pro Arg Leu Trp Leu Phe Gly Tyr Asp Glu Gln Arg
      210                      215                      220

```

132

Gln Pro Leu Thr Val Glu His Met Tyr Glu Asp Ile Ser Gln Asp His  
225 230 235 240

Val Lys Lys Thr Val Thr Ile Glu Asn His Pro His Leu Pro Pro Pro  
245 250 255

Pro Met Cys Ser Val His Pro Cys Arg His Ala Glu Val Met Lys Lys  
260 265 270

Ile Ile Glu Thr Val Ala Glu Gly Gly Gly Glu Leu Gly Val His Met  
275 280 285

Tyr Leu Leu Ile Phe Leu Lys Phe Val Gln Ala Val Ile Pro Thr Ile  
290 295 300

Glu Tyr Asp Tyr Thr Arg His Phe Thr Met  
305 310

&lt;210&gt; 179

&lt;211&gt; 2379

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 179

```

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ccatagttta aaatcgaata gtgccatcat cacagtatat tagtcaaata gaagcttcat 180
cagaaatgta tcccacatag agttttaaga cttggattct cttctgccct tgtaatctc 240
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atctgatgct gtgtccaaaa ttatgcactg tttgttgaag tagaaccaga aatcctgacc 360
tcctgttaaa tgacatcagt tccccctct gagcaacaga ctgcttgtct tgctaggaga 420
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ccaaacacag atttctcttc tagcacttta gaattgatcc ttgaagtctc tcctggttca 600
ttcaaataca agctgtgtga gtctggtgat ttctgtgat tggctctaatg tgagctcttt 660
gaacagacag atctgacagt ggaatgactc tccccgtct ctggcataac tgctttgcc 720
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actcctgtaa tcccagcact ttgggaggcc cagtgaggtg ggagaattgc ttgaaccag 2280
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<210> 180
<211> 67
<212> PRT
<213> Homo sapiens
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<400> 180
Met Gly Asp Trp Thr Trp Leu Tyr Arg Val Gly Cys Phe Phe Leu Ser
  1             5             10             15
Ala Ile Thr Cys His Ser Ile Leu Cys Ser Pro Arg Arg Met Val Ser
      20             25             30
Ala Phe Ser Cys Arg Cys Met Pro Ser Glu Pro Arg Asn Thr Lys Tyr
      35             40             45
Ile Gly Leu Lys Arg Glu Thr Gln Gly Cys Gln Phe Ser Val Gly Leu
  50             55             60

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Pro Leu Pro  
65

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<210> 181
<211> 1607
<212> DNA
<213> Homo sapiens
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<400>	181						
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attttcatgc	tttcttttagt	atttattacc	atcataccga	ttcaaaactat	tttattgtct	180	
aatacattag	catttttgat	tttgatggaa	attgttacag	aattttaaga	tttgatgaaa	240	
taagatgtag	cagatttttt	gtagcaagtt	tctggtaaaa	gggtttttttg	caagtctcag	300	
gttcttgcgtg	cactat	ttttaaatat	tattccagt	tattctaatt	cagaagcatt	360	
cttttcaagt	aacagcagca	cttgtgaaa	gaaaaa	tgccatgtt	tcttagtagg	420	
ttactaaatt	tgtacaatta	attaagattt	tagccatcag	tgagtttgaa	aaggggaaatg	480	
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attgtaccaa	ctcctctggc	ctcctctccc	tcaattaaaa	aaacacactt	accagttttg	720	
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<210> 182  
<211> 58



&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 182

Met Tyr Leu Phe Ser Ala Leu Lys Cys Phe Gln Lys Ile Lys Leu Leu  
 1 5 10 15

Leu Phe Val Cys Phe Phe Asn Arg Asn Val Asp Gly Glu Ile Gly Gly  
 20 25 30

Asn Leu Ser Ile Gly Thr Ala Thr Leu Ser Ser Leu Gly Leu Lys Glu  
 35 40 45

Lys Val Asn Leu Met Pro Arg Gly Glu Gln  
 50 55

&lt;210&gt; 183

&lt;211&gt; 2695

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 183

gaacagagta gtagccaggc aatgtttctca taataaacag aaaaggaaaa gaaactccaa 60  
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 tctaagtatg agagatatgt ttaatatatt tttatgggct gaaaaccctg agtgggaaaa 360  
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 taaaagttca ttttttctgg atgggtatgt gtatgtgtgt gtgtctgtcy aygtgtgtat 480  
 gttttatgag cttgttaaca ctaatgtcat acaaaagtac tggttagcag gaataagatt 540  
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 tgactaatct ccttttaaga tttaggcatt tactgtgtga aatatgtggc acattttcca 720  
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135

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 agaaaactat gcacaaaata aaattcaagg atgaaaaata aaaaaaaaaa aaaaa 2695

&lt;210&gt; 184

&lt;211&gt; 256

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; UNSURE

&lt;222&gt; (64)

&lt;400&gt; 184

Met Ile Thr Phe Leu Pro Ile Ile Phe Ser Ile Leu Val Val Val Thr  
 1 5 10 15

Phe Val Leu Gly Asn Phe Ala Asn Gly Phe Ile Val Leu Val Asn Ser  
 20 25 30

Ile Glu Trp Val Lys Arg Gln Lys Ile Ser Phe Ala Asp Gln Ile Leu  
 35 40 45

Thr Ala Leu Ala Val Ser Arg Val Gly Leu Leu Trp Val Ile Leu Xaa  
 50 55 60

His Trp Tyr Ala Thr Val Leu Asn Pro Gly Ser Tyr Ser Leu Gly Val  
 65 70 75 80

Arg Ile Thr Thr Ile Asn Ala Trp Ala Val Thr Asn His Phe Ser Ile  
 85 90 95

Trp Val Ala Thr Ser Leu Ser Ile Phe Tyr Leu Leu Lys Ile Ala Asn  
 100 105 110

Phe Ser Asn Phe Ile Phe Leu His Leu Lys Arg Arg Ile Lys Ser Val  
 115 120 125

Ile Pro Val Ile Leu Leu Gly Ser Leu Leu Phe Leu Val Cys His Leu  
 130 135 140

Val Val Val Asn Met Asp Glu Ser Met Trp Thr Lys Glu Tyr Glu Gly  
 145 150 155 160

Asn Val Ser Trp Glu Ile Lys Leu Ser Asp Pro Thr His Leu Ser Asp  
 165 170 175

Met Thr Val Thr Thr Leu Ala Asn Leu Ile Pro Phe Thr Leu Ser Leu  
 180 185 190

Leu Ser Phe Leu Leu Leu Ile Cys Ser Leu Cys Lys His Leu Lys Lys  
 195 200 205

Met Gln Phe His Gly Lys Gly Ser Pro Asp Ser Asn Thr Lys Val His  
 210 215 220

Ile Lys Ala Leu Gln Thr Val Thr Ser Phe Leu Leu Leu Phe Ala Val  
 225 230 235 240

136.

Tyr Phe Leu Ser Leu Ile Thr Ser Ile Trp Asn Phe Arg Arg Arg Leu  
 245 250 255

<210> 185  
 <211> 1111  
 <212> DNA  
 <213> Homo sapiens

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 tgcattgagac ccacagactc ttgcaagctg gatgccctct gtggatgaaa gatgtatcat 180  
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 agcaccacca catctctgtt ctaaagtgtt ttctctgca ataaaggacg tttgaattta 1080  
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 1111

<210> 186  
 <211> 290  
 <212> PRT  
 <213> Homo sapiens

<400> 186  
 Met Tyr His Gly Met Asn Pro Ser Asn Gly Asp Gly Phe Leu Glu Gln  
 1 5 10 15  
 Gln Gln Gln Gln Gln Gln Pro Gln Ser Pro Gln Arg Leu Leu Ala Val  
 20 25 30  
 Ile Leu Trp Phe Gln Leu Ala Leu Cys Phe Gly Pro Ala Gln Leu Thr  
 35 40 45  
 Gly Gly Phe Asp Asp Leu Gln Val Cys Ala Asp Pro Gly Ile Pro Glu  
 50 55 60  
 Asn Gly Phe Arg Thr Pro Ser Gly Gly Val Phe Phe Glu Gly Ser Val  
 65 70 75 80  
 Ala Arg Phe His Cys Gln Asp Gly Phe Lys Leu Lys Gly Ala Thr Lys  
 85 90 95  
 Arg Leu Cys Leu Lys His Phe Asn Gly Thr Leu Gly Trp Ile Pro Ser  
 100 105 110  
 Asp Asn Ser Ile Cys Val Gln Glu Asp Cys Arg Ile Pro Gln Ile Glu  
 115 120 125  
 Asp Ala Glu Ile His Asn Lys Thr Tyr Arg His Gly Glu Lys Leu Ile  
 130 135 140

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Ile Thr Cys His Glu Gly Phe Lys Ile Arg Tyr Pro Asp Leu His Asn  
 145 150 155 160  
 Met Val Ser Leu Cys Arg Asp Asp Gly Thr Trp Asn Asn Leu Pro Ile  
 165 170 175  
 Cys Gln Gly Cys Leu Arg Pro Leu Ala Ser Ser Asn Gly Tyr Val Asn  
 180 185 190  
 Ile Ser Glu Leu Gln Thr Ser Phe Pro Val Gly Thr Val Ile Ser Tyr  
 195 200 205  
 Arg Cys Phe Pro Gly Phe Lys Leu Asp Gly Ser Ala Tyr Leu Glu Cys  
 210 215 220  
 Leu Gln Asn Leu Ile Trp Ser Ser Ser Pro Pro Arg Cys Leu Ala Leu  
 225 230 235 240  
 Glu Gly Gly Arg Pro Glu His Leu Phe Pro Val Leu Tyr Phe Pro His  
 245 250 255  
 Ile Arg Leu Ala Ala Ala Val Leu Tyr Phe Cys Pro Val Leu Lys Ser  
 260 265 270  
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 275 280 285  
 Leu Phe  
 290

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 <213> Artificial Sequence

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 <223> oligonucleotide

<220>  
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 <222> (2)  
 <223> biotinylated phosphoramidite residue

<400> 187  
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29

<210> 188  
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 <212> DNA  
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<220>  
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<220>  
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<400> 188

tncagaaaga ctgcagggat tcgggacaa 29

<210> 189  
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<220>  
<223> oligonucleotide

<220>  
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<223> biotinylated phosphoramidite residue

<400> 189  
antcatcact acacgtcttc tcccctaca 29

<210> 190  
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<213> Artificial Sequence

<220>  
<223> oligonucleotide

<220>  
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<400> 190  
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<210> 191  
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<220>  
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<400> 191  
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<210> 192  
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<220>  
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<400> 192  
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29

<210> 193  
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<220>  
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<400> 193  
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29

<210> 194  
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<212> DNA  
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<220>  
<223> oligonucleotide

<220>  
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<222> (2)  
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<400> 194  
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29

<210> 195  
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<212> DNA  
<213> Artificial Sequence

<220>  
<223> oligonucleotide

<400> 195  
gcatatactc tgttgcccgc

20

<210> 196  
<211> 18  
<212> DNA  
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<220>  
<223> oligonucleotide

<400> 196  
ctgccactat ccccaggg

18

<210> 197  
<211> 29  
<212> DNA  
<213> Artificial Sequence

<220>  
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<220>  
<221> misc\_feature  
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<223> biotinylated phosphoramidite residue

<400> 197  
antggtgtgc cactcccaac aatctttcc

29

<210> 198  
<211> 2505  
<212> DNA  
<213> Homo sapiens

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cttgagggcg tagggccgag accgtcgcggt gtactgaggc gcctccgctc tctctcccac 180  
tcgcccggccg ctttccaaga catatgtccc gcttgccagc catttcgatg ctgcgaaacg 240  
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aataagaagg agaacaaaga agttattctt aaacttctgg tcatatttga gaacataaat 1920  
gataatttca aatgggaaga aaatgaacct actcagaatc aattcggtga aggttcactt 1980  
tttttctttt taaaagaatt tcaagtgtgt gctgataagg ttctgggaat agaaagtcac 2040  
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&lt;223&gt; biotinylated phosphoramidite residue

&lt;400&gt; 221

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29

&lt;210&gt; 222

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Pro Ser Leu Asp Val Cys Thr Asn Tyr Ser Leu Glu Leu Phe Ser Leu  
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Ala Leu Gln Leu Leu Pro Pro Thr Ser Ser Pro Ala Pro Pro Ile His  
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Ser Phe Ala  
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 Met Asn Val Tyr Thr His Phe Arg Gly Ser His Gln Gly Gln Val Gln  
     1                    5                    10                    15  
 Gly Ser Gly Pro Ser Gly Trp Cys Leu Gln Gly Asn Phe Gly Pro Ser  
           20                    25                    30  
 Leu Phe Ser Asp Trp Arg Ser Pro Trp Pro Ala Ser Phe His Thr Xaa  
       35                    40                    45  
 Leu Leu Ala Gly Thr Gly Leu Ala Pro Thr Phe Pro Ala Ser Ser Val  
       50                    55                    60  
 Val Ala Ser Leu Pro Glu Pro Gly Ser Ser Ser Gly Pro Thr Ser Lys  
       65                    70                    75                    80  
 Cys His

<210> 276  
 <211> 130  
 <212> PRT  
 <213> Homo sapiens

<400> 276  
 Met Asp Asp Met Leu Ser Thr Arg Ser Ser Thr Leu Thr Glu Asp Gly  
     1                    5                    10                    15  
 Ala Lys Ser Ser Glu Ala Ile Lys Glu Ser Ser Lys Phe Pro Phe Gly  
           20                    25                    30  
 Ile Ser Pro Ala Gln Ser His Arg Asn Ile Lys Ile Leu Glu Asp Glu  
       35                    40                    45  
 Pro His Ser Lys Asp Glu Thr Pro Leu Cys Thr Leu Leu Asp Trp Gln  
       50                    55                    60  
 Asp Ser Leu Ala Lys Arg Cys Val Cys Val Ser Asn Thr Ile Arg Ser  
       65                    70                    75                    80  
 Leu Ser Phe Val Pro Gly Asn Asp Phe Glu Met Ser Lys His Pro Gly  
           85                    90                    95  
 Leu Leu Leu Ile Leu Gly Lys Leu Ile Leu Leu His Lys His Pro  
       100                    105                    110  
 Glu Arg Lys Gln Ala Pro Leu Thr Tyr Glu Lys Glu Glu Glu Gln Asp  
       115                    120                    125  
 Gln Gly  
       130

161

&lt;210&gt; 277

&lt;211&gt; 111

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 277

Met Leu Gly Tyr Arg Lys Ile Asn Ala Lys Ala Lys His Pro Val Pro  
 1 5 10 15

Val Leu Glu Val Pro Arg Gly Arg Met Pro Arg Leu Arg Lys Lys Leu  
 20 25 30

Leu Ser Trp Pro Gly Gln Arg Glu Glu Glu Pro Arg Val Gly Val Val  
 35 40 45

Thr His Leu Lys Ile Thr Met Ser Ser Gly Arg Cys Ala Ile Val Leu  
 50 55 60

Gly Leu Gly Gly Cys Gly Arg Pro Thr Leu Gly Met Gln Ser Ser Asp  
 65 70 75 80

Ser Val Ser Leu Ala Thr Leu Gly Leu Leu Thr Thr Leu Pro Val Leu  
 85 90 95

Leu Thr Leu Arg Glu Gly Ser Cys Trp Val Asp Ser Arg Gln Ala  
 100 105 110

&lt;210&gt; 278

&lt;211&gt; 104

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 278

Met Glu Asn Ser Leu Leu Ala Met Phe His Glu Ser Arg Ile Leu His  
 1 5 10 15

Leu Trp Ala Ala Leu Phe Leu Val Glu Leu Leu Gln Glu Val Pro Ile  
 20 25 30

Met Thr Cys Ser Asn Ala Asn Thr Pro Ser Val Asn Thr Gly Tyr Phe  
 35 40 45

Lys Leu Ser Ser Val Ala Thr Thr Leu Arg Gln Gln Gln Leu Val Leu  
 50 55 60

Glu Ile Ser Leu Met Ser Val Pro Pro Gly Cys Gly Pro Leu Leu Pro  
 65 70 75 80

Val Leu Ile Pro Val Ala Ser Phe Cys Cys Ile Ile Thr Ile Trp Leu  
 85 90 95

Leu Ile Leu Met Phe Glu Lys Asp  
 100

&lt;210&gt; 279

&lt;211&gt; 147

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

162.

&lt;400&gt; 279

Met Ala Ser Pro Ser Gly Leu Cys Val Leu Val Arg Leu Pro Lys Leu  
 1 5 10 15  
 Ile Cys Gly Gly Lys Thr Leu Pro Arg Thr Leu Leu Asp Ile Leu Ala  
 20 25 30  
 Asp Gly Thr Ile Leu Lys Val Gly Val Gly Cys Ser Glu Asp Ala Ser  
 35 40 45  
 Lys Leu Leu Gln Asp Tyr Gly Leu Val Val Arg Gly Cys Leu Asp Leu  
 50 55 60  
 Arg Tyr Leu Ala Met Arg Gln Arg Asn Asn Leu Leu Cys Asn Gly Leu  
 65 70 75 80  
 Ser Leu Lys Ser Leu Ala Glu Thr Val Leu Asn Phe Pro Leu Asp Lys  
 85 90 95  
 Ser Leu Leu Leu Arg Cys Ser Asn Trp Asp Ala Glu Thr Leu Thr Glu  
 100 105 110  
 Asp Gln Val Ile Tyr Ala Ala Arg Asp Ala Gln Ile Ser Val Ala Leu  
 115 120 125  
 Phe Leu His Leu Leu Gly Tyr Pro Phe Ser Arg Asn Ser Pro Gly Glu  
 130 135 140  
 Lys Lys Arg  
 145

&lt;210&gt; 280

&lt;211&gt; 176

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 280

Met Thr Asp Cys Leu Val Ile Lys His Phe Leu Arg Lys Ile Ile Met  
 1 5 10 15  
 Val His Pro Lys Val Arg Phe His Phe Ser Val Lys Val Asn Gly Ile  
 20 25 30  
 Leu Ser Thr Glu Ile Phe Gly Val Glu Asn Glu Pro Thr Leu Asn Leu  
 35 40 45  
 Gly Asn Gly Ile Ala Leu Leu Val Asp Ser Gln His Tyr Val Ser Arg  
 50 55 60  
 Pro Asn Phe Gly Thr Ile Glu Ser His Cys Ser Arg Ile His Pro Val  
 65 70 75 80  
 Leu Gly His Pro Val Met Leu Phe Ile Pro Glu Asp Val Ala Gly Met  
 85 90 95  
 Asp Leu Leu Gly Glu Leu Ile Leu Thr Pro Ala Ala Ala Leu Cys Pro  
 100 105 110  
 Ser Pro Lys Val Ser Ser Asn Gln Leu Asn Arg Ile Ser Ser Val Ser  
 115 120 125

163

Ile Phe Leu Tyr Gly Pro Leu Gly Leu Pro Leu Ile Leu Ser Thr Trp  
 130 135 140

Glu Gln Pro Met Thr Thr Phe Phe Lys Asp Thr Ser Ser Leu Val Asp  
 145 150 155 160

Trp Lys Ile Pro Phe Val Tyr Asp Thr Gln Phe Gly Ser Gln Phe Gly  
 165 170 175

&lt;210&gt; 281

&lt;211&gt; 89

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 281

Met Gly Ser Leu Ser Thr Ala Asn Val Glu Phe Cys Leu Asp Val Phe  
 1 5 10 15

Lys Glu Leu Asn Ser Asn Asn Ile Gly Asp Asn Ile Phe Phe Ser Ser  
 20 25 30

Leu Ser Leu Leu Tyr Ala Leu Ser Met Val Leu Leu Gly Ala Arg Gly  
 35 40 45

Glu Thr Ala Glu Gln Leu Glu Lys Val Leu His Phe Ser His Thr Val  
 50 55 60

Asp Ser Leu Lys Pro Gly Phe Lys Asp Ser Pro Lys Cys Ser Gln Ala  
 65 70 75 80

Gly Arg Ile His Ser Glu Phe Gly Val  
 85

&lt;210&gt; 282

&lt;211&gt; 115

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 282

Met Val Thr Gly Met Leu Ile Ser Ser Thr Arg Gly Ser Ser Asp Gly  
 1 5 10 15

Arg Asn Cys Ser Ala Ile Leu Val Pro Val Ser Pro Val Gly Arg Gln  
 20 25 30

Pro Leu Tyr Leu Thr Ser Arg Pro Gly Asp Trp Ser Gln Gly Tyr Cys  
 35 40 45

Thr Thr Gly Gln Phe Pro Ala Ile Val Arg Lys Glu Thr Pro Glu Leu  
 50 55 60

Asn Gly Arg Asp Ile Pro Ala Val Phe Asn Ile Thr Pro Met Pro Phe  
 65 70 75 80

Val Arg Leu Pro Cys Thr Glu Ile Thr Trp Arg Ala Ser Cys Arg Leu  
 85 90 95

Tyr Leu Arg Thr Leu Val Lys Tyr Leu Leu Ser Phe Leu Ala Ala Arg  
 100 105 110

164

Met Gln Lys  
115

<210> 283

<211> 189

<212> PRT

<213> Homo sapiens

<400> 283

Met Val His Cys Pro His Glu Leu Leu Gln Met Pro Leu Ser Leu Phe  
1 5 10 15

Ser Gln Arg Ser Trp Val Thr Gln Cys Leu Asp Thr Trp Lys Thr Cys  
20 25 30

Thr Leu Ile Thr Gln Arg His Leu Ala Ser Asp His Leu Pro Ser Glu  
35 40 45

Phe Leu Leu Val Gln Leu Gly Tyr His Pro Leu Thr His Gln Ala Ala  
50 55 60

Pro His Leu Pro Leu Leu Leu Leu Trp Gln Val Phe Pro Ala Tyr Gln  
65 70 75 80

Glu Gln Gly Phe Ser Cys Lys Gly Gln Leu Leu Leu Gly Leu Leu Val  
85 90 95

Ser Thr Asp Asn Ile Phe Leu Pro Ile Leu Gly Gln Ala Pro Gln Thr  
100 105 110

His Pro Leu Leu Pro His Gln Arg Trp Ala Asn Gln Lys Glu Ser Val  
115 120 125

Pro Val Lys Ile Glu Arg Tyr Leu Pro Gln Leu Glu Gln Arg Asp Trp  
130 135 140

Pro Glu Phe Gly Lys Glu Gly Leu Leu His Lys Pro Arg Arg Gly Pro  
145 150 155 160

Val Leu Ser Leu Pro Leu Asp Thr Val Glu Ser Gly His Leu Val Ser  
165 170 175

Met Leu Cys Gln Lys Ala Tyr Gln Val Gly Arg Asn Leu  
180 185

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1/20, 15/63, 5/00

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HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,  
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,  
MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,  
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patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,  
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Published:

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(54) Title: SECRETED PROTEINS AND POLYNUCLEOTIDES ENCODING THEM

(57) Abstract: Novel polynucleotides and the proteins encoded thereby are disclosed.



**WO 01/075068 A3**



## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/09369

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) :Please See Extra Sheet.

US CL :Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : *Please See Extra Sheet*

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Database: N_Geneseq_1101; Accession NO: AAX60801; Agostino et al., "Human secreted protein encoding DNA (clone bd306_7)"; 09 August 1999; having 100% sequence identity to SEQ ID NO: 1; see entire document.	1, 2, 7, 8
X	Database: A_Geneseq_1101; Accession NO: AAY17219; Agostino et al.; "Human secreted protein (clone bd306_7); 09 August 1999; having 99.9% sequence identity to SEQ ID NO: 2; see entire document.	1, 2, 7, 8



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier document published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	"&" document member of the same patent family

Date of the actual completion of the international search

07 JUNE 2002

Date of mailing of the international search report

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/09369

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99/26961 A1 (GENETICS INSTITUTE, INC) 03 JUNE 1999,see entire document,especially pages 51 and 57.	1-5, 7, 8
X	Database: SPTREMBL_17; Accession NO: O75718; Castagnola et al. " Cartilage-associated protein (CASP) precursor"; 01 November 1998; having 99.9% sequence identity to SEQ ID NO: 2; see entire document.	1, 2, 7

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US01/09369

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-5, 7, 8

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US01/09369

## A. CLASSIFICATION OF SUBJECT MATTER:

IPC (7):

C07H 21/02, 21/04; C07K 5/00, 14/00; C12Q 1/68; C12P 21/06, C12N 1/20, 15/63, 5/00

## A. CLASSIFICATION OF SUBJECT MATTER:

US CL :

536/23.1, 23.5, 24.31; 530/300, 350; 435/6, 69.1, 252.3, 320.1, 325

## B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

Sequence Search (Database: GenEmbl, N\_Geneseq\_1101, Issued\_Patents\_NA, EST, A\_Geneseq\_1101, Issued\_Patents\_AA, Pir\_6,8 SwissProt\_39, SPTREMBL\_17)

STN (Database: CA, CAPLUS, USPATFULL)

DIALOG (Database: MEDLINE, BIOSIS, DIALOG GLOBAL REPORTER, DERWENT WPI)

Search Terms: polynucleotide, polypeptide, secreted protein, transmembrane protein

## BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I. Claims 1-5, 7, 8, directed to an isolated polynucleotide comprising or related to nucleotide sequence of SEQ ID NO: 1 that encodes a protein of SEQ ID NO: 2, vector, host cell and a process of producing the protein recombinantly.

Group II. Claims 6, 9-12, directed to an isolated protein comprising or related to amino acid sequence of SEQ ID NO: 2, a composition comprising the protein related to SEQ ID NO: 2.

Group III. Claim 13, directed to an isolated polynucleotide comprising or related to the nucleotide sequence of SEQ ID NO: 19.

Group IV. Claim 14, directed to an isolated protein comprising or related to amino acid sequence of SEQ ID NO: 20.

and it considers that the International Application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups I-IV do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The polynucleotides and polypeptides of each of the clones bd306\_7 and ybd\_1 in the claims are unrelated, each to the other. The polynucleotide sequences encode structurally distinct polypeptides and do not share a special technical feature. Furthermore, the technical feature that links the DNA, protein, methods of cDNA clone bd306\_7 (claim 1) is not a contribution over the prior arts of Agostino et al. and Castagnola et al. See the various documents cited in the search report. Thus the technical feature of the polynucleotide sequence is not special and the groups are not so linked under PCT Rule 13.1. Additionally the claimed methods produce different products and/or different results which are not coextensive and which do not share the same technical feature.